G 51/2

United States
Environmental Protection
Agency

Air Risk Information
Support Center
Research Triangle Park NC 27711

EPA/450/3-88/016

Air

EPA

Glossary of Terms Related to Health, Exposure, and Risk Assessment

Air RISC
AIR RISK INFORMATION SUPPORT CENTER

EP 4.2:

READEX FICHE best copy available

EPA/450/3-88/016
March 1989

Glossary of Terms Related to Health, Exposure, and Risk Assessment

by

Air Risk Information Support Center (Air RISC)
U.S. Environmental Protection Agency

Sponsored by:

Office of Air Quality Planning and Standards
Research Triangle Park, NC 27711

Office of Health and Environmental Assessment
Research Triangle Park, NC 27711
Cincinnati, OH 45268
Washington, DC 20460

Center for Environmental Research Information
Cincinnati, OH 45268

Disclaimer

This report has been reviewed by the Office of Air Quality Planning and Standards of the Office of Air and Radiation, and by the Office of Health and Environmental Assessment and the Center for Environmental Research Information of the Office of Research and Development and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the U.S. Environmental Protection Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

Contents

		Page
Introduction		iv
1.	Glossary of Health, Exposure, and Risk Assessment Terms	1
2.	Discussion of Related Terms Frequently Encountered in Health, Exposure, and Risk Assessment	
	Cohort Compared with Case-control Studies	17
	Cohort Studies Compared with Clinical Studies	17
	Epidemiology Compared with Toxicology	18
	Parameters: Most Sensitive Compared with Most Critical Compared with Most Selective	19
	LOAEL Compared with NOAEL	19
	LD Compared with LC	19
	Additive, Synergistic, and Antagonistic Effects	20
	Mitosis and Meiosis	20
	Threshold Compared with Non-Threshold	20
	Benign Compared with Malignant	20
	Exposure Compared with Dose	21
	Sensitive Compared with Sensitization	21
	Quantal Dose-response Compared with Graded Dose-Response	21
	Epigenetic (Nonmutagenic) Carcinogens Compared with Mutagenic Carcinogens	21
	Initiators and Promoters	21
	Qualitative Compared with Quantitative Risk Assessment	22
	Risk Assessment Compared with Risk Management	22
	Population Threshold Compared with Individual Threshold	22
	Measurement Compared with Modeling	23
	Aggregate Compared with Individual Risk	23
3.	References	25

Introduction

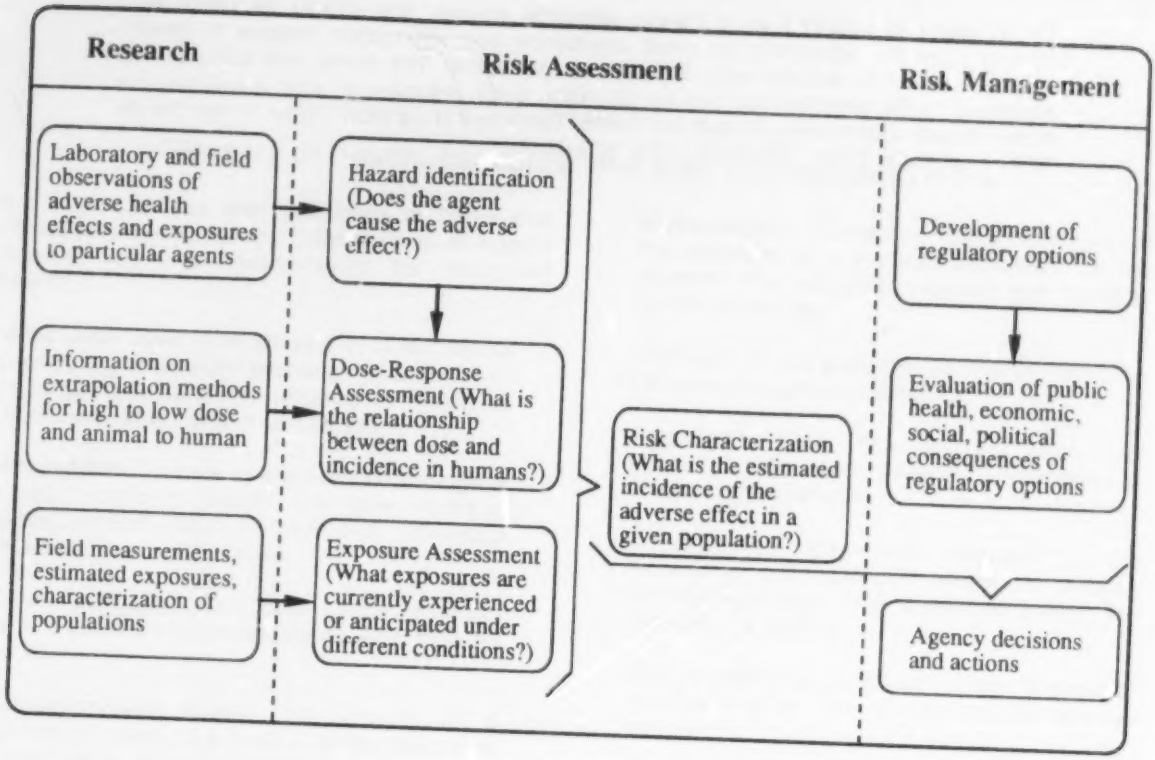
Many state and local agencies are developing or implementing programs to control emissions of toxic air pollutants. To successfully carry out these programs, agency personnel must be familiar with a wide range of issues and terms related to health, exposure, and risk assessment for toxic air pollutants. Understanding these issues and terms is not always an easy task. This glossary has been prepared by the U.S. EPA's Air Risk Information Support Center (Air RISC) as a resource tool for State and local air pollution control agencies and U.S. EPA Regional Offices. The purpose of the glossary is to define terms that are commonly used in health, exposure, and risk assessments for toxic air pollutants.

The Air RISC is operated by the U.S. EPA's Office of Air Quality Planning and Standards (OAQPS), Office of Health and Environmental Assessment (OHEA), and Center for Environmental Research Information (CERI). The key goal of Air RISC is to provide technical assistance to State and local air pollution control agencies and U.S. EPA Regional Offices in obtaining, reviewing, and interpreting air toxics data related to health, exposure, and risk assessment. Through Air RISC, Regional, State, and local agency personnel can obtain expert guidance and information on health, exposure, and risk assessment issues and methodologies.

This glossary is divided into three sections:

- *Section 1* provides brief definitions of commonly used risk assessment, exposure assessment, and biological terms.
- *Section 2* provides more detailed discussions of related terms frequently encountered in health, risk and exposure assessments.
- *Section 3* lists key references concerning health, exposure, and risk assessment for air toxics. These resources include general texts on toxicology, carcinogenicity, and risk assessment, as well as certain U.S. EPA references relating to health and exposure assessment.

The terms included in the glossary were selected by expectations of their commonality of usage relative to the elements of the risk assessment process for inhaled chemicals. The conceptual framework for risk assessment as it is currently practiced, was defined by the National Academy of Science in 1983 as a four-phase process. The elements in this process, as well as the interrelationships between research, risk assessment and risk management are shown in the following figure.


Research
Risk Assessment
Risk Management
Laboratory and field observations of adverse health effects and exposures to particular agents
Hazard identification (Does the agent cause the adverse effect?)
Information on extrapolation methods for high to low dose and animal to human
Dose-Response Assessment (What is the relationship between dose and incidence in humans?)
Field measurements, estimated exposures, characterization of populations
Exposure Assessment (What exposures are currently experienced or anticipated under different conditions?)
Risk Characterization (What is the estimated incidence of the adverse effect in a given population?)
Development of regulatory options
Evaluation of public health, economic, social, political consequences of regulatory options
Agency decisions and actions

Elements of Risk Assessment and Risk Management (From: National Academy of Sciences, [NAS] 1983

As indicated by the figure, a number of types of information are used in health risk assessment. Hazard identification is a qualitative determination that a given agent is causally linked to particular health effects. Data evaluated in this process may include epidemiologic, animal studies, short-term assays and structure activity comparisons. The exposure assessment component uses information on environmental levels, fate and transport, ecologic analyses, applied exposures at the point of contact, any pharmacokinetic modeling of the data, and demographic characteristics. A dose-response assessment is performed by staff trained in biomedical and/or physical sciences, who use available data on health endpoints, both for human and animal studies. The assessment includes evaluation of how data from the human and animal studies is influenced by the level of exposure to the chemical agent, as well as differences between species or in target organ toxicologic responses. The final component, termed risk characterization, is the formal application of mathematical analysis to the data to estimate the individual and population risks or whether there is a threshold in dose level which is exceeded. The Risk Characterization also contains a discussion and interpretation of the numerical estimates and the degree to which the quantitative estimates are likely to reflect the true magnitude of human risk.

Introduction (continued)

The glossary is intended as a handy reference source, and should be used as a starting point for accessing technical assistance and information relative to health, exposure, and risk assessments for toxic air pollutants. The terms and comparisons presented in this directory can provide an initial, quick response to your questions. For more detailed information, consult the references listed in Section Three or call the Air RISC Hotline at (919) 541-0888; FTS 629-0888.

Section 1

Glossary of Health, Exposure, and Risk Assessment Terms

This section provides brief definitions of terms that are frequently encountered in discussions of health, exposure, and risk assessments for toxic air pollutants.

Absorbed dose. The amount of a substance penetrating across the exchange boundaries of an organism, via either physical or biological processes, after contact (exposure).

Absorption. To take in a substance through a body surface such as the lungs, gastrointestinal tract, or skin and, ultimately into body fluids and tissues.

Acute exposure. One or a series of short-term exposures generally lasting less than 24 hours.

Administered dose. The amount of a substance given to a human or test animal in determining dose-response relationships, especially through ingestion or inhalation (see applied dose). Even though this term is frequently encountered in the literature, administered dose is actually a measure of exposure, because even though the substance is "inside" the organism once ingested or inhaled, administered dose does not account for absorption (see absorbed dose).

Adverse effect. A biochemical change, functional impairment, or pathological lesion that either singly or in combination adversely affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge.

Adenoma. A benign tumor originating in the covering tissue (epithelium) of a gland.

Additivity. A pharmacologic or toxicologic interaction in which the combined effect of two or more chemicals is approximately equal to the sum of the effect of each chemical alone. (Compare with: antagonism, synergism.)

Aerodynamic diameter. A measurement of the diameter of a particle expressed as the diameter of a unit density sphere with identical inertial properties.

Aerosol. A suspension of liquid or solid particles in a gaseous medium.

Aggregate risk. The sum of individual increased risks of an adverse health effect in an exposed population.

Airway. Any conducting segment of the respiratory tract through which air passes during breathing. The bronchial tubes are examples of airways.

Airway resistance (Raw). The functional resistance to air flow afforded by the airways between the mouth and the alveoli.

Alkylation. The substitution of an alkyl radical for a hydrogen atom in a chemical molecule. An alkyl radical follows the general formula $C_nH_{2_n+1}$. Alkylation is viewed as an event that may lead to toxicity.

Allergen. An antigenic substance capable of eliciting an allergic response.

Altered growth. A change in offspring, organ, or body weight or size. Altered growth can be induced at any stage of development, may be reversible, or may result in a permanent change.

Alveolar. Pertaining to the air sacs (alveoli) of the lung where gas exchange occurs.

Alveolar macrophage. A cell within the lung that contributes to immunological activities of the lung by phagocytosing (engulfing) and killing microbes, phagocytosing inhaled particles, secreting/excreting antimicrobial substances, and performing other activities. Under some conditions, it also can secrete/

excrete enzymes capable of digesting lung tissue.

Alveolar ventilation. The volume of air entering the alveoli each minute.

Ambient. Encompassing or surrounding area.

Ames test. An *in vitro* bacterial test for detecting point mutations in a group of histidine-requiring strains of *Salmonella typhimurium*. An Ames test is usually conducted with an exogenous source of metabolic activation by adding, for example, enzymes obtained from mammalian liver cells (S9 liver fraction), to the *S. typhimurium* assay system.

Anaphylaxis. An exaggerated reaction to an antigen to which an organism has been previously sensitized.

Anemia. A condition characterized by a reduction in the number of circulating red blood cells and/or the number of hemoglobin molecules in red blood cells.

Anergy. Diminished reactivity to specific antigens.

Aneuploidy. A condition in which the chromosome number is not an exact multiple of the usual number of chromosomes for that species. For example, a "normal" human has 46 chromosomes; an individual with 47 chromosomes would be described as aneuploid.

Annual incidence. The number of new cases of a disease occurring or predicted to occur in a population over a year.

Anoxia. Absence/lack of or significant reduction in oxygen.

Antagonism. A pharmacologic or toxicologic interaction in which the combined effect of two chemicals is *less than* the sum of the effect of each chemical alone; the chemicals either interfere with each other's actions, or one interferes with the action of the other. (Compare with: additivity, synergism.)

Antibody. A protein substance developed in response to, and interacting specifically with, an antigen. The antibody-antigen reaction forms a major basis for immunity.

Antigen. A substance that induces the formation of antibodies and interacts with its specific antibody. Antigens may be introduced into the body or may be formed within the body. The antigen-antibody reaction forms a basis for immunity.

Apnea. Temporary cessation of breathing.

Applied Dose. The amount of a substance given to a human or test animal in determining dose-response relationships, esp. through dermal contact (see administered dose). Even though this term is encountered in the literature, applied dose is actually a measure of exposure, since it does not take absorption into account.

Arrhythmia. Any variation from the normal rhythm of the heartbeat.

Asthma. A condition marked by recurrent attacks of difficult or labored breathing and wheezing resulting from spasmodic contraction and hypersecretion of the bronchi resulting from exposure to allergens such as drugs, foods, environmental pollutants, or intrinsic factors.

Atmospheric half-life. The time required for one-half of the quantity of an air pollutant to react and/or break down in the atmosphere.

Atmospheric residence time. The time required for removal of a substance from the atmosphere to the extent that 1/e (approximately 37%) of the original material remains.

Atrophy. Reduction in the size of a structure or organ resulting from lack of nourishment or functional activity, death and reabsorption of cells, diminished cellular proliferation, pressure, ischemia or hormone changes.

Averaging time. The time period over which a function (e.g., average concentration of an air pollutant) is measured, yielding a time-weighted average.

Benign. A condition of a neoplasm (tumor) in which the morphological and behavioral characteristics of the tumor differ minimally from the tissue from which it originates. A benign neoplasm (as distinct from malignant) may expand, but remains encapsulated, and has limited potential to invade local structure and proliferate.

Bioaccumulation. Progressive increase in amount of a chemical in an organism or part of an organism that occurs because the rate of

intake exceeds the organism's ability to remove the substance from the body.

Bioassay. A test conducted in living organisms to determine the hazard or potency of a chemical by its effect on animals, isolated tissues, or microorganisms.

Bioavailability. A measure of the degree to which a dose of a substance becomes physiologically available to the body tissues depending upon absorption, distribution, metabolism and excretion rates.

Bioconcentration. Same as bioaccumulation; refers to the increase in concentration of a chemical in an organism.

Biological half-life. The time required for the concentration of a chemical present in the body or in a particular body compartment to decrease by one-half through biological processes such as metabolism and excretion.

Biological markers/monitoring. Measuring chemicals or their metabolites in biological materials (e.g., blood, urine, breath) to estimate exposure, or to detect biochemical changes in the exposed subject before or during the onset of adverse health effects. Sometimes refers to a specific indicator for a particular disease/functional disturbance.

Biologically significant effect. A response in an organism or other biological system that is considered to have a substantial or noteworthy effect (positive or negative) on the well-being of the biological system. Used to distinguish statistically significant effects or changes, which may or may not be meaningful to the general state of health of the system.

Biotransformation. An enzymatic chemical alteration of a substance within the body that generally leads to a more excretable metabolite, sometimes producing a more toxic form of the substance.

Block group/enumeration district (BG/ED). The smallest geographic areas used by the Bureau of Census in conducting the population census. Block groups are designated for urban areas, while enumeration districts are designated for rural areas. BG/EDs data are frequently incorporated into exposure models to estimate population exposure to environmental pollutants.

Bronchial. Pertaining to the airways of the lung below the larynx that lead to the alveolar region of the lungs. Bronchial airways provide a passageway for air movement.

Bronchiectasis. Pathological dilation of a bronchus or of the bronchial tubes.

Bronchitis. Inflammation of the mucous membrane of the bronchial tubes.

Cancer. A malignant new growth. Cancers are divided into two broad categories: carcinoma and sarcoma.

Carcinogenic. Able to produce malignant tumor growth. Operationally most benign tumors are usually included also.

Carcinogenic process. A series of stages at the cellular level after whichcancer will develop in an organism. Some believe there are at least 3 stages: initiation, promotion, and progression.While hypothesized as staged process, little is known about specific mechanisms of action.

Carcinoma. A malignant tumor of epithelial cell origin (e.g., skin, lung, breast), tending to infiltrate the surrounding tissue and give rise to metastases.

Case-control study. A retrospective epidemiologic study in which individuals with the disease under study (cases) are compared with individuals without the disease (controls) in order to contrast the extent of exposure in the diseased group with the extent of exposure in the controls.

Ceiling limit. A concentration limit in the work place that should not be exceeded, even for a short time, to protect workers against frank health effects.

Central nervous system. The portion of the nervous system that includes the brain and spinal cord, and their connecting nerves.

Chemical mixture. Any combination of two or more substances regardless of source or of spatial or temporal proximity.

Chromosome. A very long molecule of DNA complexed with protein, containing genetic information arranged in a linear sequence.

Chromosome abnormality. A group of conditions associated with abnormalities in the number or structure of chromosomes. These can be produced by insertion, deletion, or rearrangement of chromosomal segments.

Chronic exposure. Long-term exposure usually lasting six months to a lifetime.

Chronic obstructive pulmonary disease (COPD). A disease of the lung, involving increased resistance to air flow in the bronchial airways and loss of tissue elasticity, that leads to decreased ability of the lungs to perform ventilation. The pathological changes that lead to COPD can be caused by chronic bronchitis, pulmonary emphysema, chronic asthma, and chronic bronchiolitis.

Cirrhosis. A liver disease characterized by increased fibrous tissue, accompanied by other abnormal physiological changes. Clinical signs of cirrhosis include the loss of functional liver cells and increased resistance to blood flow through the liver.

Ciliated epithelial cell. A cell with cilia that lines the tracheobronchial region of the lung. The beating of the cilia moves mucus and substances (such as inhaled particles trapped on/in the mucus) upwards and out of the lung, thereby contributing significantly to lung clearance.

Clastogenic. Able to break chromosomes and thereby produce chromosome abnormalities, a form of genotoxicity. This results in the gain, loss, or rearrangement of pieces of chromosomes.

Clearance. The disappearance of a compound from a specific organ or body compartment or the whole body. In pulmonary toxicology, clearance refers specifically to removal of an inhaled substance that deposits on the lung surface.

Cohort study. A study of a group of persons sharing a common experience (e.g., exposure to a substance) within a defined time period; this experiment is used to determine if an increased risk of a health effect (disease) is associated with that exposure.

Complete carcinogen. Chemicals that are capable of inducing tumors in animals or humans without supplemental exposure to other agents. Complete refers to the three stages of carcinogenesis, initiation, promotion, and progression which need to be present in order to induce a cancer.

Compliance. Pulmonary compliance. The volume change per unit of pressure change for the lungs, the thorax, or the lungs-thorax system. The distensibility of the lungs or thorax.

Confidence limit. The confidence interval is a range of values that has a specified probability (e.g., 95 percent) of containing a given parameter or characteristic. The confidence limit refers to the upper value of the range (e.g. upper confidence limit).

Control group. A group of subjects observed in the absence of the exposure agent for comparison with exposed groups.

Critical Endpoint. A chemical may elicit more than one toxic effect (endpoint), even in one test animal, in tests of the same or different duration (acute, subchronic, and chronic exposure studies). The doses that cause these effects may differ. The critical endpoint used in the dose-response assessment is the one that occurs at the lowest dose. In the event that data from multiple species are available, it is often the most sensitive species that determines the critical endpoint. This term is applied in the derivation of risk reference doses.

Cross-sectional study. An epidemiologic study assessing the prevalence of a disease in a population. These studies are most useful for conditions or diseases that are not expected to have a long latent period and do not cause death or withdrawal from the study population. Potential bias in case ascertainment and exposure duration must be addressed when considering cross-sectional studies.

Cyanosis. Bluish discoloration, especially of the skin and mucous membranes and fingernail beds caused by deficient oxygenation of the blood.

Cytochrome P-448 and P-450. Enzymes which are important in the detoxification by biotransformation of many chemical substances. Cytochrome P-448 and P-450 enzymes, integral in the metabolic activation and detoxification of many compounds, are found primarily in the liver and, to a lesser extent, in the lung and other tissues.

Cytotoxicity. Producing a specific toxic action upon cells.

DNA. Deoxyribonucleic acid. The nucleic acid molecule in chromosomes that contains the genetic information. The molecule is double stranded, with a "backbone" of phosphate and

sugar (deoxyribose) to which the nucleotide bases are attached. The nucleotides form a ladder-like structure by hydrogen bonds such that adenine (A) pairs with thymine (T) and guanine (G) pairs with cytosine (C). The specific sequence of nucleotide bases defines the gene.

DNA adduct. A lesion in the DNA formed by the covalent binding of an exogenous chemical to one of the nucleotide bases. DNA adducts are frequently the precursors to changes in the sequence of nucleotides (mutations).

DNA crosslink. A lesion in the DNA formed by the covalent binding of an exogenous chemical to two nucleotide bases, one each on opposing strands of the DNA. DNA crosslinks usually prevent DNA replication and are lethal to cells attempting to divide.

Deposition. Specific to air toxics, the adsorption on the respiratory tract surface of inhaled, gaseous, or particulate pollutants. Also, adsorption of a gaseous or particulate air pollutant at the surface of the ground, vegetation, or water.

Dermatitis. Inflammation of the skin.

Detoxification. Reduction of a chemical's toxic properties by means of biotransformation processes, to form a more readily excreted, or a less toxic chemical than the parent compound.

Developmental toxicity. Adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism. Major manifestations of developmental toxicity include: death of the developing organism; induction of structural abnormalities (teratogenicity); altered growth; and functional deficiency.

Diffusion. Movement of a chemical substance from areas of high concentration to areas of low concentration. Biologically, diffusion is an important means for toxicant deposition for gases and very small particles in the pulmonary region of the lungs.

Diploid. The chromosome state in which each homologous chromosome is present in pairs. Normal human somatic (non-reproductive) cells are diploid (i.e., they have 46 chromosomes), whereas reproductive cells, with 23 chromosomes are haploid.

Dispersion model. A mathematical model or computer simulation used to predict the movement of airborne pollution. Models take into account a variety of mixing mechanisms which dilute effluents and transport them away from the point of emission.

Disposition. The movement and fate of chemicals in the body, including absorption, distribution, biotransformation, and excretion.

Distribution. Transport of a substance through the body by physical means (e.g., active transport or diffusion). Distribution is dependent on the chemical properties of the toxicant or its metabolites and, to some extent, the route of exposure as well as physiologic variables.

Diuresis. Increased production of urine.

Dose-response relationship. A relationship between: (1) the dose, often actually based on "administered dose" (i.e., exposure) rather than absorbed dose, and (2) the extent of toxic injury produced by that chemical. Response can be expressed either as the severity of injury or proportion of exposed subjects affected. A dose-response assessment is one of the four steps in a risk assessment.

Dosimetry. In general, the measurement or modeling of the amount, rate, and distribution of a drug or toxicant especially as it pertains to producing a particular biological effect.

Dyspnea. Difficult or labored breathing.

Edema. An accumulation of an excessive amount of fluid in cells, tissues, or serous cavity. Lung edema is the accumulation of fluid in the lung.

Embryo. In mammals, the stage in the developing organism at which organs and organ systems are developing. For humans, this involves the stage of development between the second through eighth weeks (inclusive) post conception.

Embryotoxicity. Any toxic effect on the conceptus as a result of prenatal exposure during the embryonic stages of development. These effects may include malformations and variations, altered growth, in utero death, and altered postnatal function.

Emphysema. Chronic pulmonary disease characterized by loss of lung function due to

destruction of many of the alveolar walls with resulting enlargement of the air spaces. The total epithelial area for gas exchange in the lungs is reduced in emphysema patients.

Endemic. Present in a community or among a group of people; said of a disease prevailing continually in a region.

Endocrine. Pertaining to hormones or to the glands that secrete hormones into the blood.

Endothelial. Pertaining to the layer of flat cells lining the inner surface of blood and lymphatic blood vessels, and the surface lining of serosa and synovial membranes.

Endpoint. An observable or measurable biological or chemical event used an an index of the effect of a chemical on a cell, tissue, organ, organism, etc.

Environmental Fate. The destiny of a chemical or biological pollutant after release into the environment. Environmental fate involves temporal and spatial considerations of transport, transfer, storage, and transformation.

Epidemiology. The study of the occurrence and distribution of a disease or physiological condition in human populations and of the factors that influence this distribution.

Epigenetic. Alterations in the expression of genes by mechanisms other than changes in the nucleotide sequence of DNA. The term has historically been used in the area of embryonic differentiation, but more recently has been used in describing a component of the formation of cancer.

Epithelial. Pertaining to the cell layer that covers all internal and external surfaces of the body, including the gastrointestinal, respiratory, and urinary tracts.

Equilibrium. The state in which opposing forces are exactly counteracted or balanced. Types of equilibrium include acid-base, colloid, dynamic, homeostatic, and chemical. Used in risk assessment of toxic air pollutants to generally describe the chemical equilibrium between a pollutant in the inhaled air and the level in the body.

Excess risk. An increased risk of disease above the normal background rate.

Excretion. Elimination or discharge of excess and waste chemicals from the body. Chemicals may be excreted through feces, urine, exhaled breath, etc..

Exposure. Contact of an organism with a chemical, physical, or biological agent. Exposure is quantified as the amount of the agent available at the exchange boundaries of the organism (e.g., skin, lungs, digestive tract) and available for absorption.

Exposure assessment. Measurement or estimation of the magnitude, frequency, duration and route of exposure of animals or ecological components to substances in the environment. The exposure assessment also describes the nature of exposure and the size and nature of the exposed populations, and is one of four steps in risk assessment.

Extrapolation. An estimate of response or quantity at a point outside the range of the experimental data. Also refers to the estimation of a measured response in a different species or by a different route than that used in the experimental study of interest (i.e., species-to-species, route-to-route, acute-to-chronic, high-to-low).

Extrathoracic. Situated or occurring outside the thorax (the part of the respiratory tract above the trachea).

Fence Line Concentration. Modeled or measured concentrations of air pollutants found at the boundaries of a property on which a pollution source is located. Usually assumed to be the nearest location at which an exposure of the general population could occur.

Fertility. The ability to achieve conception and to produce offspring. For litter-bearing species, the number of offspring per litter is also used as a measure of fertility. Reduced fertility is sometimes referred to as subfertility.

Fetus. The post-embryonic stage of the developing young. In humans, from the end of the second month of pregnancy up to birth.

Fibrosis. Formation of scar tissue in the lung or other tissues, usually as a result of inflammation occurring over a long period of time.

First pass effect. Reduction in a substance's systemic availability resulting from metabolism or excretion by the first major organ of contact

with such capability after the absorption process. This phenomenon of removing chemicals after absorption before entering the general systemic circulation can occur in the lung or liver.

Flash point. The lowest temperature at which a chemical will ignite.

Forced expiratory volume (FEV). The amount of air that can be forcefully exhaled in a specified time, usually one second (FEV_1). A forced expiratory volume test provides an index of lung function.

Forced vital capacity (FVC). The greatest amount of air that can be forcefully exhaled following maximum inhalation.

Frank effect level (FEL). Related to biological responses to chemical exposures (compare with NOAEL and LOEL); the exposure level that produces an unmistakable adverse health effect (such as inflammation, severe convulsions, or death).

Gamma multi-hit model. A dose-response model that can be derived under the assumption that the response is induced if the target site has undergone some number of independent biological events (hits).

Functional developmental toxicity. The study of the causes, mechanisms, and manifestations of alterations or delays in functional competence of the organism or organ system following exposure to an agent during critical periods of development pre- and/or postnatally. This is a subset of development toxicity.

Gamete. A mature male or female germ cell [sperm or ovum (egg)] usually possessing a haploid chromosome set and capable of initiating formation of a new diploid individual by fusion with a gamete from the opposite sex.

Gastrointestinal. Pertaining to the intestines and stomach.

Gavage. Experimental exposure regimen in which a substance is administered to an animal into the stomach via a tube.

Gene. The simplest complete functional unit in a DNA molecule. A linear sequence of nucleotides in DNA that is needed to synthesize a protein and/or regulate cell function. A mutation in one or more of the nucleotides in a genemay lead to abnormalities in the structure of the gene product or in the amount of gene product synthesized.

Genome. A term used to refer to all the genetic material carried by a single gamete.

Genotoxic. A broad term that usually refers to a chemical which has the ability to damage DNA or the chromosomes. This can be determined directly by measuring mutations or chromosome abnormalities or indirectly by measuring DNA repair, sister-chromated exchange, etc. Mutagenicity is a subset of genotoxicity.

GEMS (Graphical Exposure Modeling System). An interactive computerized management tool developed by the U.S. EPA that ties together several previously discrete tools into a coordinated system, allowing for multiple types of analyses. These tools include environmental fate and transport models, chemical property estimation techniques, statistical analysis, and graphical and modeling programs.

Germ cell. A cell capable of developing into a gamete [ovum (egg) or sperm].

Glomerulus. Part of the nephron, the basic structure of the kidney.

Half-life. See atmospheric half-life and biological half-life. Also, the period of time characteristic of a radionuclide in which one-half of the activity has decayed.

Haploid. Containing a single set of unpaired chromosomes. Gametes (specialized reproductive cells) are characterized as haploid. (Compare with: diploid.)

Hazard identification. The process of determining whether exposure to a substance is causally related to the incidence and/or severity of an adverse health effect (e.g., cancer, birth defects, etc.). Hazard identification involves gathering and evaluating data on the types of health injury or disease that may be produced by a chemical and on the conditions of exposure under which injury or disease is produced. It may also involve characterization of the behavior of a chemical within the body and the interactions it undergoes within organs, cells, or even parts of cells. Hazard identification is the first step in the risk assessment process.

Hemangiosarcoma. A malignant neoplasm characterized by rapidly proliferating, extensively infiltrating, anaplastic cells derived

from blood vessels and lining blood-filled spaces.

Hema or Hemo. Prefix, pertaining to blood.

Hemoglobin. The oxygen-carrying protein in red blood cells.

Hepato. Prefix, pertaining to the liver.

Histology. The discipline that deals with the structure of cells, tissues, and organs in relation to their function.

Homeostasis. Maintenance of normal, internal stability in an organism by coordinated responses of the organ systems.

Hormone. A chemical substance, formed in one organ or part of the body and carried in the blood to another organ or part where it alters the functional activity, and sometimes the structure, of one or more organs by its specific chemical activity.

Host defense(s)/systems. A complex system that defends the body against biological or chemical agents. Often referred to with respect to the lungs where the system clears the lungs of microbes and particulate pollutants. Also refers to chemical defenses such as antioxidant substances that defend against oxidants such as ozone or nitrogen dioxide.

Human equivalent dose. The human dose of an agent expected to induce the same type and severity of toxic effect that an animal dose has induced.

Human Exposure Model (HEM). A mathematical model used in exposure assessments for toxic air pollutants to quantify the number of people exposed to pollutants emitted by stationary sources and the pollutant concentrations they are exposed to. Input data include plant characteristics such as location, emission, parameters, etc. as well as Bureau of Census data used in the estimation of persons exposed and appropriate meteorological data.

Hygroscopic. Absorbing moisture from the air.

Hyper. Prefix, pertaining to a higher than normal value.

Hyperplasia. The abnormal multiplication or increase in the number of normal cells in normal arrangement in a tissue.

Hypersensitivity. Exaggerated response by the immune system to an allergen. Sometimes used incorrectly in a non-immune sense to indicate increased susceptibility to the effects of a pollutant.

Hypertension. Abnormally elevated arterial blood pressure.

Hypertrophy. Enlargement of an organ due to increase in cell size with no change in the cell number. For example, liver hypertrophy occurs in mice exposed to chlorinated hydrocarbons or to phenobarbital.

Hyperventilation. Overventilation; increased rate of air exchange relative to metabolic carbon dioxide production so that alveolar carbon dioxide pressure tends to fall below normal.

Hypo. Prefix, pertaining to a less than normal value.

Hypoxia. Low oxygen content in a body tissue(s); below physiologic levels.

Immediately dangerous to life and health (IDLH). A concentration representing the maximum level of a pollutant from which an individual could escape within 30 minutes without escape-impairing symptoms, or irreversible health effects.

Immune system. All internal structures and processes providing defense against disease causing organisms (viruses, bacteria, fungi, parasites). Includes nonspecific defense mechanisms, such as interferon production, epithelialmembranes and phagocytic cells, as well as specific immune responses of cells producing antibodies in response to antigens entering the body.

Immunodeficiency. A condition resulting from ineffective functioning of the immunological system. Immunodeficiency may be primary (due to a defect in the immune mechanism per se) or secondary (dependent upon another disease process or toxicant exposure).

Immunosuppression. Decrease of immunologic response, usually resulting from exposure to chemical, pharmacologic, physical, or immunologic agents.

Incidence. The number of new cases of a disease within a specified time period. It is frequently presented as the number of new cases per 1,000, 10,000, or 100,000. The incidence rate is a direct estimate of the

probability or risk of developing a disease during a specified time period.

Individual risk. The increased risk for a person exposed to a specific concentration of a toxicant.

Indoor/outdoor ratio. The ratio of the indoor concentration of an air pollutant to the outdoor concentration of that pollutant.

Industrial Source Complex (ISC) model. A Gaussian dispersion model used to predict the movement of a plume of air pollution and concentrations the general population may be exposed to near a facility. There are two versions of the ISC model, short-term and long-term. This is a standard model used by the U.S.EPA and incorporates detailed source and emissions characteristics and appropriate meteorological data.

Infertile. Lacking fertility, inability to conceive offspring. Infertility may be temporary or permanent; permanent infertility is termed sterility.

Inflammation. A protective tissue response to injury that serves to destroy, dilute, or wall off both the injurious agent and the injured tissue. It is characterized by symptoms such as pain, heat, redness, swelling and loss of function. Under some circumstances, it can be a toxic response due to local accumulations of cells and mediators.

Initiator. An agent capable of starting but not necessarily completing the process of producing an abnormal, uncontrolled growth of tissue usually by altering a cell's genetic material. Initiated cells may or may not be transformed into tumors.

Interspecies. Between different species.

Interspecies scaling factors. Numerical values used in the determination of the equivalent doses between species, (e.g. frequently a known animal dose is scaled to estimate an equivalent human dose.) The U.S. EPA's cancer risk assessment guidelines (50 FR 33992) note that commonly used dosage scales include milligram per kilogram body weight per day, parts per million in soil or water or air, milligram per square meter body surface area per day, and milligram per kilogram body weight per lifetime. The guidelines for carcinogen assessment generally recommend using the surface area approach unless there is evidence to the contrary. The dose as mg/kg of body weight/day is generally used to scale between species for non-cancer effects of chemicals after dermal, oral, or parenteral exposure.

Intramuscular. Within the muscle; refers to injection.

Intraperitoneal. Within the membrane surrounding the organs of the abdominal cavity; refers to injection.

Intraspecies. Within a particular species.

Intravascular. Within the blood vessels; refers to injection, usually into the veins (intravenous or i.v.).

in vitro. Tests conducted outside the whole body in an artificially maintained environment, as in a test tube, culture dish, or bottle

in vivo. Tests conducted within the whole living body.

Lacrimation. Secretion and discharge of tears.

Larynx. The enlarged upper end of the trachea, below the root of the tongue commonly referred to as the voice box.

Latency. The period of time between exposure to an injurious agent and the manifestation of a response.

Lavage. A technique used to wash out a cavity such as the stomach or a portion of the lungs via a tube. This technique is commonly used clinically to remove toxic substances from the stomach. This procedure may also be used to obtain cell populations and fluids from the lung for experimental manipulation.

Lesion. A pathologic or traumatic discontinuity of tissue or loss of function.

Lethal. Deadly; fatal.

LC_{LO} (Lethal Concentration Low). The lowest concentration of a chemical required to cause death in some of the population after exposure for a specified period of time and observed for a specified period of time after exposure. Refers to inhalation time exposure in the context of air toxics (may refer to water concentration for tests of aquatic organisms or systems).

LC_{50} (Median Lethal Concentration). The concentration of a chemical required to cause death in 50% of the exposed population when exposed for a specified time period, and

observed for a specified period of time after exposure. Refers to inhalation exposure concentration in the context of air toxics (may refer to water concentration for tests of aquatic organisms or systems).

LD_{LO} (Lethal Dose Low). The lowest dose of a chemical required to cause death in some of the population after noninhalation exposure, e.g., injection, ingestion, for a specified observation period after exposure.

LD_{50} (Median Lethal Dose). The dose of a chemical required to cause death in 50% of the exposed population after noninhalation exposure, e.g., injection, ingestion, for a specified observation period after exposure.

Leukemia. A progressive, malignant disease of the blood-forming tissues, marked by an excessive number of white blood cells and their precursors.

Lifetime. Covering the lifespan of an organism (generally considered 70 years for humans).

Limited evidence. According to the U.S. EPA carcinogen risk assessment guidelines, limited evidence is a collection of facts and accepted scientific inferences that suggests the agent may be causing an effect but the suggestion is not strong enough to be an established fact.

Local effect. A biological response occurring at the site of first contact between the toxic substance and the organism.

Logit model. A dose-response model that can be derived under the assumption that the individual tolerance level is a random variable following the logit distribution.

Lower respiratory tract. That part of the respiratory tract below the larynx.

Lowest-observed-adverse-effect level (LOAEL). The lowest dose or exposure level of a chemical in a study at which there is a statistically or biologically significant increase in the frequency or severity of an adverse effect in the exposed population as compared with an appropriate, unexposed control group.

Lowest-observed effect level (LOEL). In a study, the lowest dose or exposure level at which a statistically or biologically significant effect is observed in the exposed population compared with an appropriate unexposed control group.

Lymphoma. Any abnormal growth (neoplasm) of the lymphoid tissues. Lymphoma usually refers to a malignant growth and thus is a cancer.

Macrophage. A specialized cell of the immune system capable of engulfing and digesting foreign particles.

Male reproductive toxicity. The occurrence of adverse effects on the male reproductive system, which may result from exposure to environmental agents. The toxicity may be expressed as alterations to the male reproductive organs and/or the related endocrine system. The manifestation of such toxicity may include alteration in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of the male reproductive system.

Malformation. A permanent structural change in a developing organism that may adversely affect survival, development, or function. Compare with variation.

Malignant. A condition of a neoplasm (tumor) in which it has escaped normal growth regulation and has demonstrated the ability to invade local or distant structures, thereby disrupting the normal architecture or functional relationships of the tissue system.

Margin of exposure (MOE). The ratio of the no-observed-adverse-effect level (NOAEL) to the estimated human exposure. The MOE was formerly referred to asthe margin of safety (MOS).

Margin of safety (MOS). The term formerly applied to the margin of exposure concept.

Mass median aerodynamic diameter (MMAD). Median of the distribution of mass with respect to the aerodynamic diameter of a particle.

Maximum individual risk (MIR). The increased risk for a person exposed to the highest measured or predicted concentration of a toxicant.

Maximum likelihood estimate (MLE). A statistical best estimate of the value of a parameter from a given data set.

Maximum tolerated dose (MTD). The highest dose of a toxicant that causes toxic effects without causing death during a chronic

exposure and that does not decrease the body weight by more than 10%.

Meiosis. Cell and nuclear division in which the number of chromosomes is reduced from diploid (2n) to haploid (n). This process is characteristic of germ cells (spermatocyte or oocyte) division in which two successive divisions of the nucleus produce four cells that contain half the number of chromosomes present in the somatic cells. Each of the four daughter cells obtain, at random, any one of the two copies of each chromosome from parent cell. These cells may mature to sperm or egg cells.

Metabolism. The biochemical reactions by which energy is made available for the use of an organism. Metabolism includes all chemical transformations occurring in an organism from the time a nutrient substance enters, until it has been utilized and the waste products eliminated. In toxicology, metabolism of a toxicant consists of a series of chemical transformations that take place within an organism. A wide range of enzymes act on toxicants, that may increase water solubility, and facilitate elimination from the organism. In some cases, however, metabolites may be more toxic than their parent compound.

Metaplasia. The abnormal transformation of an adult, fully differentiated tissue of one kind into a differentiated tissue of another kind.

Metastasis. The transfer of a disease, or its local manifestations, from one part of the body to another. In cancer, this relates to the appearance of neoplasms in parts of the body remote from the site of the primary tumor. This is a characteristic of malignancy.

Microbe/microorganism. A single-cell organism such as a virus or a bacterium.

Microenvironment. The immediate local environment of an organism.

Minute volume. Volume of air breathed per minute, usually liters/minute. The product of the tidal volume (the normal volume of air moved into and out of the lungs with each breath) and the respiratory rate.

Mitosis. Cellular and nuclear division that involves duplication of the chromosomes of a parent cell, and formation of two daughter cells. This type of cell division occurs in most somatic cells.

MLE. See maximum likelihood estimate.

Model. A mathematical representation of a natural system intended to mimic the behavior of the real system, allowing description of empirical data, and predictions about untested states of the system.

Modifying factor (MF). A factor that is greater than zero and less than or equal to 10; used in the operational derivation of a reference dose. Its magnitude depends upon an assessment of the scientific uncertainties of the toxicological data base not explicitly treated with standard uncertainty factors (e.g., number of animals tested). The default value for the MF is 1.

Morbidity. The number of sick individuals or cases of disease in a population.

Morphology. Study of the form or structure of cells, tissues, organs, or organisms.

Morphometry. Quantitative measure of morphology.

Mortality. The number of individual deaths in a population.

Multistage model. A mathematical function used to extrapolate the probability of incidence of disease from a bioassay in animals using high doses, to that expected to be observed at the low doses that are likely to be found in chronic human exposure. This model is commonly used in quantitative carcinogenic risk assessments where the chemical agent is assumed to be a complete carcinogen and the risk is assumed to be proportional to the dose in the low region.

Mutagenic. Ability to cause a permanent change in the structure of DNA. More specific than, but often used interchangeably with, genotoxic.

Mutation. Changes in the composition of DNA, generally divided according to size into "gene mutations" (changes within a single gene) and "chromosome mutations" (affecting larger portions of the chromosome, or the loss or addition of an entire chromosome). A "heritable mutation" is a mutation that is passed from parent to offspring and therefore was present in the germ cell of one of the parents. Somatic cell mutations may result in cancer.

Narcosis. A disorder characterized by drowsiness or unconsciousness, caused by the

action of a toxicant on the central nervous system.

Nasopharyngeal region. The area including the nasopharynx, oropharynx, and nose. The pharynx is the cavity situated between the nasal cavities, mouth, and larynx, where it divides to form the trachea and esophagus, which accept air and food, respectively.

Necrosis. Death of areas of tissue or bone, usually as individual cells, as groups of cells, or in localized areas. Necrosis can be caused by cessation of blood supply, physical agents such as radiation, or chemical agents.

Neonatal. Newly born; in humans, up to 6 weeks of age.

Neoplasia. The pathologic process that results in the formation and growth of a tumor, i.e., a neoplasm.

Neoplasm. A new and abnormal growth of tissue, such as a tumor.

Nephritis. Inflammation of the kidney.

Nephron. The structural and functional unit of the kidney, consisting of capillaries and tubes that adjust the composition of blood and form urine.

Nephro-. Prefix, pertaining to the kidney.

Neuropathy. Functional disturbances and/or pathological changes in the peripheral nervous system.

Neurotoxicity. Ability to damage nervous tissue.

Nonthreshold toxicant. An agent considered to produce a toxic effect from any dose; any level of exposure is deemed to involve some risk. Usually used only in regard to carcinogenesis.

No-observed-adverse-effect level (NOAEL). The highest experimental dose at which there is no statistically or biologically significant increases in frequency or severity of adverse health effects, as seen in the exposed population compared with an appropriate, unexposed population. Effects may be produced at this level, but they are not considered to be adverse.

No-observed-effect level (NOEL). The highest experimental dose at which there is no statistically or biologically significant increases in frequency or severity of toxic effects seen in the exposed compared with an appropriate, unexposed population.

Nucleus. The structure within the cell that contains the chromosomes and the nucleolus. The nucleus controls cellular function, both chemical reactions that occur in the cell, and reproduction of the cell. Also, the part of an atom containing protons and neutrons.

Obligate nose breathers. Animals that must breathe through the nose rather than through the mouth. Beyond the infant stage, humans may breathe either through the nose or mouth but this difference is significant when comparing effects between obligate nose breathers (e.g., rats, mice) and humans as the nasopharyngeal region can remove a proportion (often significant) of inhaled toxicants before they reach the lungs. When humans breathe through the mouth, this early removal does not occur. Infant humans are obligate nose breathers.

Occupational exposure limit (OEL). A generic term denoting a variety of values and standards, generally time-weighted average concentrations of airborne substances to which a worker can be exposed during defined work periods.

Oocyte. The immature ovum.

Oncogene. A naturally occurring gene that specifies the synthesis of a protein which is involved in normal cellular processes. Alterations in the structure or function of oncogenes are associated with the development of some cancers.

Oncogenesis. The origin and growth of a neoplasm.

One-hit model. A mathematical model that assumes a single biological event can initiate a response.

Organogenesis. The development of specific body structures or organs from undifferentiated tissue. In humans, this relates primarily to weeks 2 through 8 (inclusive) post conception.

Organoleptic. Affecting or involving an organ, especially a sense organ as of taste, smell, or sight.

Ovum. The female sex cell or gamete (egg).

Peripheral nervous system. The portion of the nervous system outside of the brain and

spinal cord, which includes sense organs and the nerves controlling the body.

Pharmacokinetics. The field of study concerned with defining, through measurement or modeling, the absorption, distribution, metabolism, and excretion of drugs or chemicals in a biological system as a function of time.

Pharynx. Passageway for air from the nasal cavity to the larynx and for food from the mouth to the esophagus.

Physiologically based pharmacokinetics. Pharmacokinetics (see above) based on measured physiological variables such as blood flows through organs, etc.

Population variability. The concept of differences in susceptibility of individuals within a population to toxicants due to variations such as genetic differences in metabolism and response of biological tissue to chemicals.

Portal of entry effects. Biological response at the site of entry (e.g., the lungs, stomach) of a toxicant into the body.

Potency. A comparative expression of chemical or drug activity measured in terms of the relationship between the incidence or intensity of a particular effect and the associated dose of a chemical, to a given or implied standard or reference.

Prevalence. The percentage of a population that is affected with a particular disease at a given time.

Probit model. A dose-response model that can be derived under the assumption that individual tolerance is a random variable following log normal distribution.

Promotion. The second hypothesized stage in a multistage process of cancer development. The conversion of initiated cells into tumorigenic cells.

Proteinuria. An excess of serum proteins in the urine.

Pulmonary region. The area of the respiratory system consisting of respiratory bronchioles and alveoli where gas exchange occurs.

q_1^* The symbol used to denote the 95% upper bound estimate of the linearized slope of the dose-response curve in the low dose region as determined by the multistage model.

Reactivity. Tendency of a substance to undergo chemical change.

Reference dose (RfD). An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive subpopulations) that is likely to be without deleterious effects during a lifetime. The RfD is reported in units of mg of substance/kg body weight/day for oral exposures, or mg of substance/m^3 of air breathed for inhalation exposures.

Renal toxicity. Ability to damage kidney cells; kidney toxicity.

Reportable quantity. The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) one pound, or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 311 of the Clean Water Act. Reportable quantities are measured over a 24-hour period.

Reproductive toxicity. Harmful effects on fertility, gestation, or offspring, caused by exposure of either parent to a substance.

Residual volume. The volume of air remaining in the lungs after a maximal forceful exhalation.

Respiratory rate. The frequency of a complete cycle of a breath (inhalation and exhalation).

Restrictive lung disease Lung disease in which the expansion of the lung is restricted either because of alterations in the supportive structures of the lung (parenchyma) or because of disease of the pleura, the chest wall, or the neuromuscular apparatus. An example is fibrosis.

Retention. The state of being held in a specific location. Used to refer to the amount of an inhaled material that remains in the lung (pulmonary retention) or to the amount of a toxicant dose that remains in the body or body compartment for a specified period of time.

RfD. See reference dose.

Risk. The probability of injury, disease, or death under specific circumstances. In quantitative terms, risk is expressed in values ranging from zero (representing the certainty

that harm will not occur) to one (representing the certainty that harm will occur).

Risk assessment. The scientific activity of evaluating the toxic properties of a chemical and the conditions of human exposure to it in order both to ascertain the likelihood that exposed humans will be adversely affected, and to characterize the nature of the effects they may experience. May contain some or all of the following four steps:

- ***Hazard identification*** - The determination of whether a particular chemical is or is not causally linked to particular health effect(s).
- ***Dose-response assessment*** - The determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question.
- ***Exposure assessment*** - The determination of the extent of human exposure.
- ***Risk characterization*** - The description of the nature and often the magnitude of human risk, including attendant uncertainty.

Risk characterization. The final step of a risk assessment, which is a description of the nature and often the magnitude of human risk, including attendant uncertainty.

Risk management. The decision-making process that uses the results of risk assessment to produce a decision about environmental action. Risk management includes consideration of technical, scientific, social, economic, and political information.

Risk-specific dose. The dose corresponding to a specified level of risk.

Route of exposure. The means by which toxic agents gain access to an organism (e.g., ingestion, inhalation, dermal exposure, intravenous, subcutaneous, intramuscular, intraperitoneal administration).

Sarcoma. A malignant tumor arising in connective tissue and composed primarily of anaplastic cells resembling supportive tissue.

SCE. See sister chromatid exchange.

Sedimentation. Deposition of particles in the small airways of the lungs which occurs as gravity acts on particles in a downward direction and buoyancy and air resistance act in an upward direction. Also, the settling out of particles in the atmosphere due to their gravitational fall.

Sensitization. An allergic condition that usually effects the skin or lungs. Once exposure to a substance has caused a reaction, the individual may be sensitized to that substance and further exposure even at low levels may elicit an adverse reaction.

Serosa. A membrane producing a serous secretion, or containing serum or a serumlike substance.

Short-term exposure limit (STEL). A time-weighted average OEL that the American Conference of Government and Industrial Hygienists (ACGIH) indicates should not be exceeded any time during the work day. Exposures at the STEL should not be longer than 15 minutes and should not be repeated more than 4 times per day. There should be at least 60 minutes between successive exposure at the STEL.

Sister chromatid exchange (SCE). The reciprocal exchange of chromosomal material between two chromatids (longitudinal subunits of a replicated chromosome). Increased SCE is indicative of genotoxic effects.

Somatic cells. All cells other than germ cells or gametes.

Spermatozoan. **Sperm**. The male sex cell or gamete.

Spirometry. The measurement of air volumes of the lungs. (Example, tidal volume, reserve volume, etc.).

Squamous cell carcinoma. A malignant neoplasm derived from squamous epithelium.

Standardized Mortality Ratio. The number of deaths, either total or cause-specific, in a given group expressed as a percentage of the number of deaths that could have been expected if the group has the same age and sex specific rates as the general population. Used in epidemiologic studies to adjust mortality rates to a common standard so that comparisons can be made among groups.

Statistically significant effect. In statistical analysis of data, a health effect that exhibits differences between a study population and a control group that are unlikely to have arisen by chance alone.

STEL. See short-term exposure limit.

Structure-activity relationship. Relationships of biological activity or toxicity of a chemical to its chemical structure or substructure.

Subcutaneous. A method of exposure where the substance is injected beneath the skin.

Subchronic exposure. Exposure to a substance spanning approximately 10% of the lifetime of an organism.

Surface area scaling factor. The intra- and interspecies scaling factor most commonly used for cancer risk assessment by the U.S. EPA to convert an animal dose to a human equivalent dose; milligrams per square meter surface area per day. Body surface area is proportional to basal metabolic rate; the ratio of surface area to metabolic rate tends to be constant from one species to another. Since body surface area is approximately proportional to an animal's body weight to the 2/3 power, the scaling factor can be reduced to milligrams per (body weight)$^{2/3}$.

Synergism. A pharmacologic or toxicologic interaction in which the combined effect of two or more chemicals is greater than the sum of the effect of each chemical alone. (Compare with: additivity, antagonism.)

Systemic. Pertaining to or affecting the body as a whole or acting in a portion of the body other than the site of entry. Used to refer generally to non-cancer effects. (Compare with portal-of-entry effects.)

Target organ/system. An organ or functional system (e.g., respiratory, immune, excretory, reproductive systems) which demonstrates toxicity to a specific chemical; not necessarily the organ/system with the highest accumulation of the chemical, but rather that which elicits a toxic response(s) of concern.

TD_{LO} (Toxic dose low). The lowest dose of a substance required to cause a toxic-effect in some of the exposed population.

Teratogenicity. The property of a chemical to cause structural or functional defects during the development of an organism.

Threshold Limit Value (TLV). The concentration of a substance below which no adverse health effects are expected to occur for workers assuming exposure for 8 hours per day, 40 hours per week. TLVs are published by the American Conference of Governmental Industrial Hygienists (ACGIH). This listing may be useful in identifying substances used in the workplace and having the potential to be emitted into the ambient air.

Threshold toxicant. A substance showing an apparent level of effect that is a minimally effective dose, above which a response occurs; below that dose no response is expected.

Tidal volume. The amount of air that is inhaled or exhaled during one breath; in humans, approximately 0.5 liter.

Time-weighted average (TWA). An approach to calculating the average exposure over a specified time period.

Toxicology. The multidisciplinary study of toxicants, their harmful effects on biological systems and the conditions under which these harmful effects occur. The mechanisms of action, detection, and treatment of the conditions produced by toxicants are studied.

Tracheobronchial region. The area of the lungs including the trachea (windpipe) and conducting airways (bronchi, bronchioles, and terminal bronchioles).

Tumor. An abnormal growth of tissue; a neoplasm.

Uncertainty. In the conduct of risk assessment (hazard identification, dose-response assessment, exposure assessment, risk characterization) the need to make assumptions or best judgments in the absence of precise scientific data creates uncertainties. These uncertainties, expressed qualitatively and sometimes quantitatively, attempt to define the usefulness of a particular evaluation in making a decision based upon the available data.

Uncertainty factor (UF). One of several, generally 10-fold factors, applied to a NOAEL or a LOAEL to derive a reference dose (RfD) from experimental data. UFs are intended to account for (a) the variation in the sensitivity among the members of the human population; (b) the uncertainty in extrapolating animal data to humans; (c) the uncertainty in extrapolating from data obtained in a less-than-lifetime exposure study to chronic exposure; and (d) the uncertainty in using a LOAEL rather than a NOAEL for estimating the threshold region.

Unit cancer risk. A measure of the probability of an individual's developing cancer as a result

of exposure to a specified unit ambient concentration. For example, an inhalation unit cancer risk of 3.0×10^{-4} near a point source implies that if 10,000 people breathe a given concentration of a carcinogenic agent (e.g., µ1 g/m^3) for 70 years, three of the 10,000 will develop cancer as a result of this exposure. In water the exposure unit is usually 1 µg/l, while in air it is 1 µg/m^3.

Upper Bound Cancer Risk-assessment. A qualifying statement indicating that the cancer risk estimate is not a true value in that the dose-response modeling used provides a value which is not likely to be an underestimate of the true value. The true value may be lower than the upper bound cancer risk estimate and it may even be close to zero. This results from the use of a statistical upper confidence limit and from the use of conservative assumptions in deriving the cancer risk estimate.

Upper respiratory tract. The structures that conduct air into the lungs, including the nasal cavity, mouth, pharynx, and larynx.

Variation. A divergency in the developing organism beyond the usual range of structural constitution that may not adversely affect survival or health. A specific category in the evaluation of developmental effects. (Compare with malformation.)

Vasoconstriction. Narrowing of a blood vessel resulting in decreased blood flow.

Ventilation. The movement of air between the lungs and the ambient air.

Vital capacity. The maximal volume of air exhaled after the deepest inspiration without forced or rapid effort. In adult humans, generally 5 liters.

Weibull model. A dose-response model of the form:

$$P(d) = 1 - \exp(-bd^m)$$

where P(d) is the probability of cancer due to a continuous dose rate d, and b and m are constants.

Weight-of-evidence. The extent to which the available biomedical data support the hypothesis that a substance causes an effect in humans. For example, the following factors increase the weight-of-evidence that a chemical poses a hazard to humans; an increase in the number of tissue sites affected by the agent; an increase in the number of animal species, strains, sexes, and number of experiments and doses showing a response; the occurrence of a clear-cut dose-response relationship as well as a high level of statistical significance in the occurrence of the adverse effect in treated subjects compared with untreated controls; a dose related shortening of thetime of occurrence of the adverse effect; etc.

Xenobiotic. A substance not normally present in the environment, such as a pesticide or pollutant.

Section 2

Discussion of Related Terms Frequently Encountered in Health, Exposure, and Risk Assessments

This section presents comparisons of related risk assessment, exposure assessment, and biological terms. Each comparison provides detailed definitions of the terms and explains how they are used in health, exposure or risk assessment.

Cohort Compared with Case-control Studies

Cohort studies are a direct approach to determining whether a given exposure increases the risk of disease. Groups that are free of the disease in question, both exposed and unexposed, but comparable in every respect that could influence risk estimation are followed through time for observation of the development of disease. Difficulties can arise from the choice of the exposed and unexposed cohorts, e.g., whether they are representative of the population from which they are selected; the expense of the undertaking and the time necessary to observe an effect, especially that of a chronic disease such as cancer. Frequently, the time to conduct the study can be shortened by proper selection of a population with documented past exposure sufficiently antecedent that the health consequences are manifest in the present.

Case-control studies are an indirect approach to evaluation of exposure versus enhanced risk of disease. Persons who have been identified as having a disease are matched with persons who are healthy, but comparable with respect to factors that might be related to the disease or the exposure. Case-control studies, intrinsically retrospective, are relatively inexpensive, quick, and most often useful for identifying suspect risk factors. The results provide direct measurement of the frequency of exposure in the diseased group versus that of the healthy controls. In some instances, the calculated exposure rates can be employed to estimate the risk of disease attributable to the suspect agent.

Thus, an individual enters a case-control study on the basis of having or not having a disease or health effect, while an individual enters a cohort study on the basis of having or not having an exposure or risk factor. The case-control study is always retrospective, while the cohort study may be either retrospective or prospective. Both types of studies use control groups.

Case-control and cohort studies each have distinct advantages and disadvantages. The cohort study can provide accurate information on exposure, can assess multiple health effects from a particular exposure, and is useful when the exposure under study can be successfully isolated. However, the cohort study is often lengthy, expensive, and may require large samples or long follow-up to observe health effects.

The case-control study is useful when the health effect under study is rare or can otherwise be isolated from other diseases, when there is a long latency period for the disease in question, and when there are multiple exposures that contribute to the disease under study. Disadvantages of the case-control study include the difficulties of reconstructing an accurate exposure history for the cases and problems in proper selection of controls.

Cohort Studies Compared with Clinical Studies

A cohort study is an epidemiologic study in which individuals are characterized by their risk factors or exposure status, and are followed forward in time to identify subsequent cases of disease or death. For example, a cohort study might follow a cohort of Vietnam veterans exposed to Agent Orange, and a control group (veterans not exposed to Agent Orange), to determine if there is an increased incidence of disease or adverse health effects in the exposed group. A cohort study may be prospective, starting from the present and going forward to a future date, or retrospective, when both the exposure and the health effect have occurred in the past.

A clinical study (also called an experimental or intervention study) has objectives that are analogous to a cohort study, except that the investigator controls or adjusts the dose (exposure) or selects the risk factor under study, and assigns the subjects, usually at random, to be either exposed to the agent under test or to a sham (control). The biological effects in the exposed group and the control group are then statistically compared; depending on the study,

individual comparisons may be made or post-exposure values may be compared with pre-exposure values for the same individual. Clinical studies are usually undertaken when there is a large body of other clinical, toxicologic, and epidemiologic evidence that points to an association between an exposure and a health outcome. Clinical studies are considered the best basis for establishing a statistical association between dose or exposure and effect in humans, since the study groups are selected randomly and the level of exposure is controlled.

Epidemiology Compared with Toxicology

Epidemiology is the study of the distribution and determinants of health and diseases in a population. A basic tenet of epidemiology is that diseases do not occur randomly, but are associated with risk factors, such as exposure to pathogens or toxicants. Historically, epidemiology developed as a way to reveal the causes of epidemics of infectious disease, such as outbreaks of cholera linked to unsanitary water supplies. Today, epidemiology is also used to discover associations between noninfectious disease or health effects (cancer, heart disease, injuries) and exposure to risk factors (e.g., environmental, occupational, diet, heredity, etc.).

Descriptive epidemiology looks at differences in disease rates among different groups, in different places, and over time to generate hypotheses about disease causation. Analytic epidemiologic studies compare two groups of people who are alike except for either (1) their exposure to a risk factor, or (2) the presence of a disease or health effect. Statistical methods are then used to determine whether an association exists between a risk factor and a disease or other health outcome. Epidemiologic studies must attempt to take into account any confounding variables of effect modifiers, which are factors that are associated with both the exposure and the health effect under study. For example, a study to determine the association between radon exposure in homes and lung cancer should take into account the smoking habits of the study populations.

While properly designed and conducted epidemiologic studies may be expensive and lengthy, they are an important source of data for risk assessments because they provide human data. Positive epidemiologic studies are generally treated as the most conclusive evidence for a particular disease. A negative result in a particular study does not mean there is no human health risk, particularly if there is evidence of the disease from animal studies.

Toxicology is the science that studies the harmful effects of substances on an organism. In toxicologic studies, scientists examine the responses of microorganisms, cells, plants, animals, or humans that have been exposed to a measured dose of a substance. Toxicologic studies provide precise information on how health effects vary with exposure levels because the exposure levels, the study population, and other experimental conditions are carefully controlled. Toxicology draws from the fields of chemistry, biochemistry, and pharmacology to investigate the metabolism and modes of action of toxic substances.

In vitro toxicologic tests, which assess the effects of toxicants on microorganisms or living cells, are a rapid and less expensive means of assessing some of the effects of a toxicant in a test system other than an intact animal or human. *In vitro* studies make use of cell culture systems, cell homogenates, perfused organs, subcellular fractions, and microorganisms. *In vivo* tests examine the effects of toxicants on intact living beings, including humans. *In vivo* studies can provide dose-response information about biological processes that involve complex metabolic pathways and interactions, endocrine and immune regulation, and multiple tissues or organs, and can help determine whether a substance can cause genetic and/or long-term effects. Both *in vitro* and *in vivo* studies are important in determining mechanisms of toxicity, that is, how a substance is absorbed into a tissue, how it interacts with tissues or other substances, and how it is metabolized and eliminated. *In vitro* studies allow the understanding of the mechanism of action in some phases of the overall metabolism and disposal of a substance.

Data from both epidemiologic and toxicologic studies are assessed qualitatively to determine the overall weight-of-evidence as to whether or not a particular chemical is potentially hazardous to humans. The qualitative assessment, also referred to as the hazard identification step of a risk assessment, should include an evaluation of the strength of the association between exposure to a toxicant and elicitation of a response (e.g., high statistical significance in relevant studies, a clear dose-response relationship, etc.), consistency (e.g., multiple species, multiple routes of exposure, etc.); and biological plausibility. This includes consideration of supportive evidence (e.g., structure activity relationships, *in vitro* tests, pharmacokinetic data, etc.). In addition to a qualitative assessment, data from epidemiologic and toxicologic studies may be used in a quantitative analysis, also referred to as the dose-response assessment step of a risk assessment.

The use of epidemiologic and toxicologic studies have limitations that must be considered. While epidemiology provides valuable data on response in human groups, it cannot assess how toxicants affect individuals, or explain individual variation within a population. *In vivo* toxicologic studies may provide information on the response of organisms to toxicants, but extrapolation from the test species to

humans is required, with all the inherent uncertainties such extrapolation implies.

Parameters: Most Sensitive Compared with Most Critical Compared with Most Selective

Changes in physiologic and biologic parameters are used by scientists to detect adverse effects resulting from exposure to toxicants. These parameters can be used to screen individuals who may be at risk due to exposure to specific toxicants. The following parameters are frequently identified:

- The *most sensitive* parameter is the effect that is first detectable following the exposure, or the effect that occurs at the lowest exposure level.
- The *most critical* parameters are indicators of the most serious health effects.
- The *most selective* parameters give scientists the most information about specific effects.

LOAEL Compared with NOAEL

The lowest-observed-adverse-effect level (LOAEL) is the lowest dose or exposure level to a chemical at which there is a statistically or biologically significant increase in the frequency or severity of adverse effects in the exposed population as compared with an appropriate control group.

The no-observed-adverse-effect level (NOAEL) is the highest dose or exposure level to a chemical at which there is no statistically or biologically significant increase in the frequency or severity of an adverse effect observed between the exposed population and its appropriate control group. Effects may be produced at this level, but, based on scientific judgment, they are not considered to be adverse (such as the appearance of a dull coat on a laboratory rat or the change of an enzyme activity in blood).

The NOAEL is often used to obtain a quantitative estimate of exposure levels at which no adverse effects are expected to occur in humans. Generally, more than one species is studied, and the highest dose at which the most sensitive species shows no adverse effect is divided by appropriate uncertainty factors to derive a reference dose (RfD). It should be noted that the NOAEL gives no quantitative or qualitative indication of toxicity that occurs above the NOAEL. In the absence of an identifiable NOAEL, a LOAEL may be used to derive an RfD. In this case, an additional uncertainty factor would be used to account for calculating from a LOAEL versus a NOAEL.

LD Compared with LC

The LD_{50} (Median Lethal Dose) is the single *dose* (i.e., mg/kg) of a toxicant that will cause death in 50% of the exposed animals over a specified observation period. This test is generally used when the route of administration is oral, dermal, or parenteral (e.g., intravenous, subcutaneous, intramuscular), and is usually the first experiment performed with a new chemical. Different doses that are estimated to produce between 10 and 90% mortality are administered to test groups of animals. A dose-response curve is derived plotting the chemical concentration given (dose) versus the death rate (response). The LD_{50} is obtained from this curve using statistical procedures.

The LC_{50} (Median Lethal Concentration) is the *concentration* (i.e., parts per million) of a toxicant that will cause death in 50% of the exposed animals over a specified exposure and observation period. This test is generally used when the route of exposure is inhalation, but is also used for aquatic toxicity testing (when the exposure route is water). As with the LD_{50}, different concentrations that are estimated to produce between 10 and 90% mortality are administered to test groups of animals. A dose-response curve is generated and the LC_{50} is obtained from this curve using statistical procedures.

These tests have been used to determine the relative toxicity of various substances, i.e., categorizing chemicals in order from "extremely toxic" to "relatively harmless." For example, the LD_{50} of an "extremely toxic" substance might be 1 milligram or less per kilogram of body weight (mg/kg), while the LD_{50} of a "relatively harmless" substance might be more than 15 grams per kilogram (g/kg). However, the LD_{50} and LC_{50} are of limited usefulness for several reasons: (1) effects other than lethality (i.e., chronic effects) may be more important to consider for a particular chemical; (2) LD_{50} and LC_{50} levels are amounts that are rarely encountered in the environment; (3) LD_{50} and LC_{50} levels do not necessarily allow predictions of relative toxicity at lower doses (depending on the slope of the dose-response curve); and (4) LD_{50} and LC_{50} levels can vary widely from species to species.

The LD_{LO} (Lethal Dose Low) is the lowest dose of a substance introduced by any route other than inhalation, over any given period of time, that causes death in humans or animals over a specified observation period. The LC_{LO} (Lethal Concentration Low) is the lowest concentration of a substance in air that causes death in humans or animals. The exposure period for calculating the LC may be less than 24 hours (acute exposure) or greater than 24 hours (subchronic or chronic exposure).

Additive, Synergistic, and Antagonistic Effects

An additive effect is a pharmacologic or toxicologic interaction in which the combined effect of two chemicals is equal to the sum of the effect of each chemical given alone.

A synergistic effect occurs when the combined effect of two chemicals is greater than the sum of the effect of each chemical given alone. For example, the solvent carbon tetrachloride and ethanol each produce liver damage, but this effect is greatly enhanced if these two substances are present together.

An antagonistic effect occurs when two chemicals given together interfere with each other's actions, or one interferes with the action of the other chemical. Thus, the combined effect of two chemicals is less than the sum of the effect of each chemical given alone. Mechanisms that produce antagonistic effects include (1) change in the disposition of a toxicant; (2) interaction of two chemicals to produce a less toxic substance; (3) counterbalancing of physiologic effects; and (4) binding of two chemicals at the same receptor. The production of antagonistic effects is the basis for antidotes.

Mitosis and Meiosis

Mitosis is the division of a somatic cell into two daughter cells, which have the same chromosomal composition as the parent cell (a pair of each chromosome, or the diploid number). Mitosis is the basis for the perpetuation of genetic material in somatic cells.

Meiosis occurs when primitive germ cells (oocytes and spermatocytes) undergo two successive divisions resulting in four cells with half the normal number of chromosomes (the haploid number). Each of these cells contains, at random, only one of the two copies of each chromosome from the parent cell. These cells may mature to sperm or egg cells. The random assortment and recombination of chromosomes are responsible for the normally observed variability of individuals in a population.

Toxicants can act on the genetic material during both mitosis and meiosis. Mutations that occur during mitosis in somatic cells are not inherited by offspring but may result in cell death, or other illness, or non-hereditary developmental defects if they occur in the early embryo. Mutations that occur during meiosis can be passed on to future generations. Meiosis and mitosis are very susceptible stages for chemical toxicity.

Threshold Compared with Nonthreshold

A threshold dose is the minimally effective dose of any chemical that is observed to produce a response, (e.g., enzyme change, liver toxicity, death). For most toxic effects, except possibly for carcinogenesis, there appear to be threshold doses. The lack of observable toxic effects following exposure to concentrations below the threshold dose may be related to (1) physiologic adaptations or homeostatic mechanisms that compensate for any slight effects; (2) failure of a sufficient dose to reach the target organ; (3) normal repair processes that rapidly correct any damage that does occur; or (4) lack of sensitivity of the measurement method.

Nonthreshold substances are those substances that are known or assumed to have some risk of response at any dose above zero. While some scientists believe that thresholds exist for some carcinogens, in general, carcinogens and mutagens are classified as nonthreshold substances. This is because (1) if an effect is caused by a single, irreversible molecular interaction of a toxicant with a target cell, there would be no threshold for that toxicant. It is believed that cancer can arise from a single cell in which the DNA has been irreversibly altered (a mutagenic effect) by a very small amount of a carcinogenic substance; (2) dose-response data from many epidemiologic studies of carcinogens fit mathematical models that are linear with no apparent threshold; and (3) even if thresholds could be determined for individuals, genetic variation within a population would make it difficult to determine a no-effect threshold for a population.

Benign Compared with Malignant

A benign tumor is a neoplasm whose morphological and behavioral characteristics differ only minimally from the tissue from which it originates. A benign tumor may expand but remains encapsulated and does not invade neighboring tissues or metastasize (produce secondary growths far away from the original tumor). The presence of benign tumors may be life threatening, but not to the degree associated with malignant tumors. Experimentally, it has been argued that some benign tumors in animals may actually be an intermediate stage in the natural progression towards cancer development.

A malignant tumor is a neoplasm that shows marked cellular atypia and marked deficiency of differentiation. The cells have the properties of anaplasia, invasiveness, and metastasis. The term cancer is equated with malignant tumors.

It has not yet been definitely established whether the development of benign tumors represents a risk factor for carcinogenicity. However, EPA generally adopts the policy that the presence of benign tumors can be taken as an indication that a cancer hazard exists, unless there is evidence to the contrary. Toxicants that produce either benign or malignant tumors in laboratory animals tend to be designated as potential human carcinogens.

Exposure Compared with Dose

Exposure is an event in which an organism comes into contact with a chemical or physical agent. Exposure can occur through ingestion, inhalation, dermal absorption, or injection.

Dose is the amount of a chemical substance taken in the body. The route of exposure generally impacts the extent of absorption and therefore the absorbed dose. The quantity can be further defined in several terms of quantity, including per unit body weight, per body-surface-area of the test animal, and per region of the lung per minute.

Dose as well as exposure must be considered in assessing risk, because (1) a toxicant must reach biologic receptors to elicit a response; (2) the production of a response and the degree of response are related to the dose of the toxicant at the receptor; and (3) the exposure concentration and the route of exposure significantly affect the dose of the toxicant at the receptors.

Sensitive Compared with Sensitization

An individual is sensitive to a toxicant if he or she shows a biologic response following exposure to that substance. Sensitization is an allergic response involving the immune system. Sensitization reactions can range from minor skin irritation to death.

Quantal Dose-response Compared with Graded Dose-Response

The dose-response relationship is the relationship between the degree of response by an organism or population to a toxicant and the amount of the toxicant administered. Quantal dose-response involves those responses that are "all-or-none," such as death or development of cancer. Most animals respond in the middle portion of the dose range, with smaller numbers at the low and high extremes of the dose range.

Graded dose-responses are those responses that occur continuously over a range, such as blood pressure, enzyme level, and pathologic changes. Some graded responses can be transformed into quantal responses. The responses of a large number of test animals can be quantified and the standard deviation (measure of variability) determined.

Epigenetic (Nonmutagenic) Carcinogens Compared with Mutagenic Carcinogens

As more chemical carcinogens (usually as determined in rodent bioassays) have been tested and found negative in short-term mutagenicity tests, it has been suggested that carcinogens be classified as either mutagenic or nonmutagenic. Mutagenic carcinogens interact with and alter the primary structure of DNA, causing a heritable alteration. This includes both direct-acting chemicals which can react directly with DNA, and indirect-acting chemicals, which must be metabolically converted to a reactive form that alters the DNA, as well as other (often inorganic) chemicals, which cause incorrect replication of DNA. Somatic mutation is generally considered the first step in the carcinogenic process and mutagenic agents are often referred to as initiators.

Nonmutagenic carcinogens include those chemicals that act initially through mechanisms such as hormonal imbalance or suppression of the immune system. Ultimately, however, the effect of these nonmutagenic agents would have to become fixed as a heritable alteration for cells to progress to cancer. Also included as non-mutagenic carcinogens are chemicals referred to as promoters. These chemicals are thought to act on pre-existing genetically altered (mutated) cells (i.e. those cells having altered DNA) to complete the cancer progress.

It should be recognized that many scientists do not believe that the dichotomous classification of carcinogens into mutagenic and nonmutagenic is really indicative of mechanism of action. Indeed, there does not exist a precise set of criteria for defining nonmutagenic. The number of available genotoxicity tests is extremely large and the probability of a common data base for any but a few is very small.

Initiators and Promoters

The cancer process is now widely accepted as being a multistage process, although the precise demonstration of this remains a research pursuit. The basic components of the stages are thought to involve: *Initiation*, *Promotion*, and *Progression*. The evidence for multiple stages is based on many experimental *in vivo* and *in vitro* observations since the 1920's. *Initiators* (I) are chemical substances which can start the cancer process. Effects caused by initiators, e.g., mutagenicity, are not reversible in nature, so that once exposed a tissue is committed to possible oncogenesis. *Promoters* (P) are chemicals which enhance the chances that cancer can happen. This enhancement occurs in initiated tissues, but not in non-initiated tissues. Promoter effects seem to be reversible, require (relative to I's) large exposures to exert their promoting effects and operationally exhibit dose thresholds. I and P can happen at different times in the life history of the tissue. *Progressors* (M) are compounds which interact with initiated and promoted tissue to bring about (M)alignancy from benign tumors. A compound possessing I + P + M is called a complete carcinogen. A complete carcinogen is of greatest concern usually because no other factors need be present in normal tissue in order to start and carry through the oncogenic process. The current practice is to assume no dose, no matter how small, is safe for complete carcinogens. Current carcinogenesis models include temporal sequence: I + P + M = cancer. It should be kept in mind that each of these gross stages (I, P

and M) are further divisible by hypothesis into a number of cellular responses in the progressive loss of cellular control characteristic of cancer.

While the multistage process can be grossly observed, primarily from biomarker studies, the exact nature of the carcinogenic process is relatively unknown. The ability to clearly demonstrate that a compound has one and only one of the I, P or M characteristics is the subject of scientific research. The conventional chronic animal bioassay program, (i.e., 2 year rat or mouse bioassay) can only demonstrate that an agent is or is not carcinogenic.

Also, it has been suggested that regulatory distinctions can be made based on these carcinogenic mechanisms. However, this proposal remains controversial. Some scientists argue, for example, that many carcinogens affect both initiation and promotion, and promoters (such as dioxin) may themselves be very potent. U.S. EPA generally considers substances found to be carcinogenic in animal tests to be complete carcinogens "unless there is definitive evidence to the contrary."

Qualitative Compared with Quantitative Risk Assessment

A qualitative risk assessment, also referred to as hazard identification, attempts to answer the question: Does exposure to a specified hazard cause adverse health effects (such as cancer)? A qualitative determination of risk may entail some interpretation, such as whether animal carcinogens are presumed to be human carcinogens, or whether benign tumors in animals represent potential human carcinogenicity.

A quantitative risk assessment begins with the assessment that a hazard does cause adverse health effects, and asks the question: What is the magnitude of the risk posed by that hazard? The quantitative assessment includes development of a mathematical description of the dose-response curve, extrapolation, where necessary, from animal data to humans, estimation of human exposurelevels, and, uses all this information for estimating individual and population risks.

Like the qualitative assessment, the quantitative assessment often involves making choices among different scientifically plausible hypotheses. For example, judgments may be made as to what dose-response models should be used to extrapolate from doses used in animal tests to lower doses generally encountered by humans; or inferences may be made as to how to extrapolate exposure measurements from a small segment of a population to the entire population.

Risk Assessment Compared with Risk Management

Risk assessment is the process of determining the potential adverse health effects of human exposure to environmental hazards. Risk assessment includes four steps:

(1) *Hazard Identification.* This is the process of determining whether exposure to an agent can cause an increased incidence of adverse health effects. It involves the use of epidemiologic data, *in vitro* studies, animal studies, and comparison of molecular structure with known chemical hazards.

(2) *Dose-response Assessment.* This is the process of characterizing the relationship between the dose of a toxicant received and the incidence of adverse health effects in exposed populations. This step usually requires extrapolation of data from animal studies to humans and from high doses to low doses.

(3) *Exposure Assessment.* This is the process of measuring or estimating the intensity, duration, and frequency of human exposure to a toxicant.

(4) *Risk Characterization.* This is the final step of risk assessment and is the process of estimating the magnitude of the public health problem that results from the hazard. It involves the combination of the hazard identification, dose-response assessment, and the exposure assessment. Thus, the final expressions of health risks are derived in this step.

Risk management is the decision-making process in which an action is taken or a policy developed once a risk has been determined to exist. It integrates the risk assessment with technical, political, social, and economic issues. Risk management is also a means of setting priorities among possible actions for a toxicant or source. Risk management must take into account the uncertainties associated with various assumptions and judgments made in each step of the risk assessment process.

Population Threshold Compared with Individual Threshold

An individual threshold is the dose of a toxicant below which no health effects occur in a given individual. The population threshold is the dose of a toxicant below which no effect will occur throughout a population. The individual and population thresholds can be quite different due to genetic variability in a population, differences in age, sex, and other factors associated with differing responses to a toxicant (e.g., health status or genetic makeup). For carcinogens, many scientists believe that even if a threshold effect could be determined for individuals, it would be difficult to demonstrate a threshold for a population because of genetic differences among individuals and because of the multiplicity of human exposures.

Measurement Compared with Modeling

Measurement (monitoring may also be used to describe this process) is the process of directly ascertaining the amount or concentration of a toxicant in the environment, whereas modeling involves the use of mathematical and/or computer simulation to predict the movement and fate of environmental toxicants. Because with direct measurement (i.e., monitoring) it is often difficult to fully assess exposure, or because there are no available measurement methods, models are frequently used in environmental risk assessment to estimate exposure. The results of exposure models may be used in regulatory decision-making. However, the use of models introduces numerous uncertainties and assumptions that are not present with measurement, including use of average meteorological data and emission estimates.

Aggregate Compared with Individual Risk

The individual risk is the probability of adverse health effects occurring in a given individual as a result of exposure to a toxicant, while the aggregate risk is the probability of an increased incidence of adverse health effects in a population or specific sub-populations exposed to a toxicant. It is difficult to determine accurately individual risk from the aggregate risk because of factors such as genetic variability, age, sex, multiplicity of exposures, and other factors that affect individual response to toxicants.

Section 3
References

This section presents brief descriptions and ordering information for references that are useful in understanding health, exposure, and risk assessments for toxic air pollutants. It includes textbooks, handbooks, EPA documents, and other reference books.

Air Pollution Assessment Methodology and Modeling, Erich Weber, ed. New York: Plenum Press, 1982.

Plenum Publishers
233 Spring Street
New York, NY 10013
212-620-8000

Plenum: $65.00; no quantity discount; S&H approximately $2.00 ea/copy

Report of a NATO Committee on the Challenges of Modern Society (CCMS) pilot study on air pollution. Discusses air quality management systems, air quality modeling, and assessment methodology.

Carcinogens: Identification and Mechanisms of Action, Griffin, C. and C. Shaw, eds. Raven Press: New York, 1978.

Raven Press
1185 Avenue of the Americas
New York, NY 10036
212-930-9500

Raven: $82.50; no quantity discounts; S&H $2.00 ea/copy

A compilation of reports from the 31st Annual Symposium on Fundamental Cancer Research. Emphasis is on the identification of environmental carcinogens; mechanisms of carcinogenesis; genetics of carcinogenesis; and cellular and molecular markers of the carcinogenic process.

Casarett and Doull's Toxicology: the Basic Science of Poisons, 3rd ed. Curtis D. Klassen, Mary O. Amdur and John Doull, eds. Riverside, New Jersey: Macmillan Publishing Co., 1986.
ISBN: 0-02-364650-0

Macmillan Publishing Co.
Front and Brown St.
Riverside, NJ 08075
212-702-2000

Macmillan: $54.95/ea; no quantity discount; S&H (UPS) 6% of order

A textbook that covers the general principles of toxicology, the types of injury produced by toxins in specific organs and organ systems, specific classes of toxins, environmental toxicology, and applications of toxicology in the health sciences.

Catalog of Teratogenic Agents, 5th ed. Thomas H. Shepard. Baltimore, Maryland: Johns Hopkins University Press, 1986.
ISBN: 0-8018-3350-7

Johns Hopkins University Press
701 W. 40th Street, Suite 275
Baltimore, MD 21211

301-338-6960

Johns Hopkins: $45/ea; no quantity discount; S&H $2.50/ea copy

Lists information on teratogenicity for over 600 agents. Included in the listing are chemicals, drugs, physical factors, and viruses. Presents information on experimental data and selected literature references for each substance.

Clinical Toxicology of Commercial Products, 5th ed. Robert E. Gosselin, Harold C. Hodge, Roger Smith, and Marion N. Gleason. Baltimore, Maryland: Williams and Wilkins Co., 1984.
ISBN: 0-683-03632-7

Williams and Wilkins
428 E. Preston St.
Baltimore, MD 21201

800-638-0672

W&W: $120/ea; 10 + copies 20% discount; S&H (UPS) $3/ea copy

Provides information necessary for dealing quickly with acute chemical poisonings arising from misuse of commercial products. Provides a list of trade name products and their ingredients; addresses and phone numbers of companies for use when product descriptions are not available; sample formulas with an estimate of toxicity of each formula; toxicologic information; and recommendations for treatment and care. Also provides some information on chronic toxicity and teratogenic, mutagenic and carcinogenic effects.

Concepts of Genetics, William S. Klug and Michael R. Cummings. Columbus,Ohio: Charles E. Merrill Publishing Company, 1983.
ISBN: 0-673-18680-6

Scott Foresman
1900 East Lake Ave.
Glenview, IL 60025

312-729-3000

Scott Foresman: $41.00 each, S&H (UPS) 6% of order

A textbook presenting the basic concepts of genetics, including heredity; DNA; genetic variation; gene structure, function and regulation; and genetics of organisms and populations.

Determining Risks to Health: Federal Policy and Practice, U.S. Department of Health and Human Services, Task Force on Health Risk Assessment, 1986.

Auburn House Publ. Co.
14 Dedham St.
Dover, MA 02030-0658

508-785-2220
800-223-2665

Auburn House: Trade $32/ea; paper $16.95/ea copy

Provides description of risk assessment process and activities as practiced by the Department of Health and Human Services. Includes comparisons to framework for risk assessment defined by the National Academy of Sciences.

Dorlands Illustrated Medical Dictionary, 27th ed. W. B. Saunders, Philadelphia
ISBN: 0-7216-3154-1

Saunders
218 W. Washington Square
Philadelphia, PA 19105

800-545-2522

Saunders $38.95/ea.; S&H 6%

A widely used, comprehensive medical dictionary.

Foundations of Epidemiology, 2nd ed. A. Lilienfeld and D.E. Lilienfeld, eds. New York: Oxford University Press, 1980.
ISBN 0-19-502723-X

Oxford University Press
200 Madison Ave.
New York, NY 10016

212-679-7300

Oxford University Press, $18.95/ea., no quantity discount, S&H free if prepaid.

An introductory textbook of epidemiology with a thorough discussion of basic concepts, study design, and interpretation.

Fundamentals of Air Pollution, Arthur C. Stern, Henry C. Wohlers, Richard W.Boubel, William P. Lowry. 2nd ed. New York: Academic Press, 1984.

Academic Press, Inc.
465 S. Lincoln Drive
Troy, MO 63379

800-321-5068

Academic: $49.95; no quantity discount; no S&H charge on prepaid order

A textbook covering the elements, effects, meteorology, and control of air poilution.

Guideline on Air Quality Models (Revised). U.S. EPA Office of Air Quality Planning and Standards, Research Triangle Park, NC 27711. July 1986. Supplement A, 1988. EPA-450/2-78-027A.

Order from:

U.S. EPA Library
MD-35
Research Triangle Park, NC 27711
(919) 541-2777
FTS 629-2777

Recommends air quality modeling techniques that may be applied to air pollution control strategy evaluations and new source reviews. Intended for use by U.S. EPA regional offices in judging the adequacy of modeling analysis performed by the U.S. EPA, state and local agencies, and by industry and its consultants. Also identifies modeling techniques and data bases that the U.S. EPA considers acceptable. Makes specific recommendations concerning air quality models, data bases and general requirements for concentration estimates.

Handbook of Emergency Toxicology: A Guide for the Identification, Diagnosis, and Treatment of Poisoning, 5th ed. Sidney Kaye. Springfield, Illinois: Charles C. Thomas, 1988.
ISBN: 0-398-05403-7

Charles C. Thomas
2600 S. 1st Street
P.O. Box 19265
Springfield, IL 62794-9265

217-789-8980

CCT: $85.00/ea; 10 + copies 10% discount; 25 + copies 15%; S&H (UPS) $2/ea copy

Discusses symptoms and signs of poisoning, lethal doses, antidotes and treatment, and analyses. Includes a listing of information about approximately 170 poisons.

Handbook of Industrial Toxicology, 3rd ed. E.R. Plunkett, ed. New York: Chemical Publishing Co., Inc., 1987.
ISBN: 0-8306-0321-X

Chemical Publishing Co., Inc.
80 Eightieth Ave.
New York, NY 10011

212-255-1950

Chem Pub: $75/ea; 10 + copies 10% discount; S&H $4.50/ea copy

A quick reference source on industrial toxicology. Lists substances under commonly-used names, along with synonyms; descriptions; occupational exposure; threshold limit values; toxicity; and preventive measures.

Handbook of Poisoning, 12th ed. Robert H. Dreisbach. Los Altos, California: Lange Medical Publications, 1987.
ISBN: 0-9395--3643-3

Learning Trends
200 Old Tappan Road
Old Tappan, NJ 07675-7095

800-922-0579
(Division of Lange)

Learning Trends: $16.50/ea; 15 + copies 15% discount; S&H included

Provides a concise summary of the diagnosis and treatment of clinically important poisons, with other poisons included in tabular form.

Handbook of Toxic and Hazardous Chemicals and Carcinogens, 2nd ed. Marshall Sittig. Park Ridge, New Jersey: Noyes Data Corp., 1985.
ISBN: 0-8155-1009-8

Noyes Publications
Mill Road at Grand Avenue
Park Ridge, NJ 07656

201-391-8484

Noyes: $96.00/ea; quantity discount available; no S&H charge on prepaid order, if not prepaid 1st copy $3, each additional copy $1 per copy

Presents concise chemical and safety information on nearly 800 toxic and hazardous chemicals. Provides information such as synonyms; potential exposure; incompatibilities; permissible exposure limits; routes of entry; harmful effects; symptoms; medical surveillance; personal protection; first aid; and disposal methods.

Human Physiology, 2nd ed. Stuart Ira Fox. Dubeque, Iowa: William C. Brown, Publishers, 1987.
ISBN: 0-697-08232-6

Wm. C. Brown
2460 Kerper Blvd.
Dubeque, IA 52001

800-338-5578

Wm. C. Brown: $52.00 each

An introductory text on the physiology of the human cardiovascular, pulmonary, renal, digestive, immune, reproductive, and endocrine systems. Presents basic information in biology and chemistry for readers who lack a science background.

Identifying and Regulating Carcinogens. Office of Technology Assessment.

U.S. Government Printing Office
Superintendent of Documents
Washington, DC 20402

202-783-3238
FTS 783-3238

U.S. G.P.O. #052-003-01080-1 $11/ea

Describes policies issued by Federal agencies concerning the identification, assessment, and regulation of carcinogenic chemicals; the chemicals that have been regulated because of carcinogenic risk; the Federal government's carcinogenicity testing program; and the extent of agency action for chemicals determined to be carcinogenic.

Integrated Risk Information System, Volume I. Supportive documentation.
U.S. Environmental Protection Agency. March 1987.
EPA 600/8-86/032a

Order from:

The National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161

703-487-4600

Contains a user's guide to the Integrated Risk Information System (IRIS), a computer-housed catalog of the U.S. EPA's risk assessment and risk management information for chemical substances. The guide also contains appendices on the use of reference dose in risk assessments; the U.S. EPA's approach to risk assessment for environmental carcinogens; drinking water health advisories; and other supplementary information.

Merck Index: An Encyclopedia of Chemicals and Drugs, 10th ed. Martha Windholz, ed.
Rahway, New Jersey: Merck and Co., Inc., 1983.
ISBN: 0-911910-27-1

Merck and Co., Inc.
Professional Handbook Dept. WBC-220
P.O. Box 2000
Rahway, NJ 07065-0901

201-750-7482

Merck: $28.50/ea; 1-9 20% discount; 10 + copies 25% discount; S&H (UPS) $3/ea copy, $15 for 20 copies

Gives concise information on over 10,000 chemicals. Includes discussion of isolation, preparation, biosynthesis, physical and biological properties, pharmacological actions, uses and toxicity.

National Air Toxics Information Clearinghouse: Qualitative and Quantitative Carcinogenic Risk Assessment, U.S. Environmental Protection Agency. U.S. EPA Office of Air Quality Planning and Standards, Research Triangle Park, North Carolina, 1987b. EPA-450/5-87-003

Federal, State, and local agencies may receive free copies by calling the Clearinghouse staff at 919-541-0850; FTS 629-0850.

Describes the basic principles and assumptions associated with a qualitative and quantitative carcinogenic risk assessment. Uses several examples of quantitative risk assessments done by state and local agencies. Aimed at managers and staff members in state and local agencies concerned with the use of risk assessment for evaluating emissions of toxic air pollutants.

National Air Toxics Information Clearinghouse: How the Clearinghouse Can Help to Answer Your Air Toxics Questions, U.S. Environmental Protection Agency. Office of Air Quality Planning and Standards, Research Triangle Park, North Carolina, 1986a. EPA-450/5-86-009

Federal, State, and local agencies may receive free copies by calling the Clearinghouse staff at 919-541-0850; FTS 629-0850.

Illustrates how the National Air Toxics Information Clearinghouse can help to answer questions commonly asked by state and local agencies involved with air toxics assessment and control. Includes discussion of several problem scenarios that may be encountered by state and local agencies.

National Air Toxics Information Clearinghouse: Bibliography of Selected Reports and Federal Register Notices Related to Air Toxics. July 1988.

Federal, State, and local agencies may receive free copies by calling the Clearinghouse staff at 919-541-0850; FTS 629-0850.

Provides citations to reports and *Federal Register* notices useful in developing and operating air toxics control programs. Reports selected are published by: U.S. EPA; National Academy of Sciences; National Cancer Institute; National Institute of Environmental Health Sciences; National Toxicology Program; National Institute for Occupational Safety and Health; World Health Organization; and various state and local agencies.

NIOSH/OSHA Occupational Health Guidelines for Chemical Hazards, U.S. Dept. HHS/Public Health Service/CDC/NIOSH, U.S. Department of Labor/ OSHA. January 1981. DHHS (NIOSH) Publication No. 81-123.

For sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402.

Occupational guidelines on 397 chemicals and metals are compiled. Information on permissible exposure limits, chemical and physical properties, and health hazards is summarized. Recommendations for medical surveillance, respiratory protection, personal protection, and sanitary practices for specific chemicals that are federally regulated are provided.

Patty's Industrial Hygiene and Toxicology, 6 Part 3 Vol. Set, 3rd ed. G.D.Clayton and F.E. Clayton, eds. New York: John Wiley and Sons, 1985.
ISBN: 0-471-86137-5

John Wiley & Sons, Inc.
1 Wiley Drive 201-469-4400
Somerset, NJ 08875 Attn: Order Dept.

Wiley: $680/set; no quantity discount; S&H (UPS) $30

NOTE: This set includes Vols. 1, 2A, 2B, 2C, 3A, and 3B; ordering information for the six individual books is listed below.
A comprehensive and detailed text on industrial hygiene and toxicology. Volume 1 covers general principles, Volumes 2A, 2B and 2C cover toxicology, and Volumes 3A and 3B cover the theory and rationale of industrial hygiene practice.

Patty's Industrial Hygiene and Toxicology, General Principles, Vol. 1, 3rd ed. G.D. Clayton and F.E. Clayton, eds. New York: John Wiley and Sons, 1978.
ISBN: 0-471-16046-6

Wiley: $172/ea; no quantity discount; S&H (UPS) $5/ea book

Patty's Industrial Hygiene and Toxicology, Vol. 2A, 3rd ed. G.D. Clayton and F.E. Clayton, eds. New York: John Wiley and Sons, 1978.
ISBN: 0-471-16042-3

Wiley: $162/ea; no quantity discount; S&H (UPS) $5/ea book

Patty's Industrial Hygiene and Toxicology, Vol. 2B, 3rd ed. G.D. Clayton and F.E. Clayton, eds. New York: John Wiley and Sons, 1981.
ISBN: 0-471-07943-X

Wiley: $115/ea; no quantity discount; S&H (UPS) $5/ea book

Patty's Industrial Hygiene and Toxicology, Vol. 2C, 3rd ed. G.C.Clayton and F.E. Clayton, eds. New York: John Wiley and Sons, 1982.
ISBN: 0-471-09258-4

Wiley: $147/ea; no quantity discount; S&H (UPS) $5/ea book

Patty's Industrial Hygiene and Toxicology, The Work Environment. Vol. 3A, 2nd ed. Lewis J. Cralley and Lester J. Cralley, eds. New York: John Wiley and Sons, 1985.
ISBN: 0-471-86137-5

Wiley: $105/ea; no quantity discount; S&H (UPS) $5/ea book

Patty's Industrial Hygiene and Toxicology, The Work Environment. Vol. 3B, 2nd ed. Lewis J. Cralley and Lester J. Cralley, eds. New York: John Wiley and Sons, 1985.
ISBN: 0-471-82333-3

Wiley: $100/ea; no quantity discount; S&H (UPS) $5/ea book

Principles of Biochemistry, Albert Lehninger. New York: Worth Publishers, Inc. 1982.

Worth Publishers, Inc.
33 Irving Place 212-475-6000
New York, NY 10003

Worth: $45.95; no quantity discount, S&H $2.95 ea/copy

A textbook written for students taking their first course in biochemistry. Covers biomolecules (including the rudiments of organic chemistry relevant to biomolecules), bioenergetics and metabolism, aspects of human biochemistry, and the fundamentals of molecular genetics.

Principles of Genetic Toxicology, 2nd ed. David Brusick. New York: Plenum Press, 1987.
ISBN: 0-306-42532-7

Plenum Publishers
233 Spring Street
New York, NY 10013

212-620-8000

Plenum: $35.00/ea.

A textbook presenting basic concepts of genetics and a thorough discussion of all aspects of genetic toxicology.

Quantitative Risk Assessment for Environment and Occupational Health. William H. Hallenbeck and Kathleen M. Cunningham-Burns. Chelsea, Michigan: Lewis Publications, Inc., 1986.
ISBN: 0-87371-055-X

Lewis Publications, Inc.
121 S. Main St.
P.O. Drawer 519
Chelsea, MI 48118

800-525-7894

Lewis: $35.95/ea; quantity discounts available; no S&H charges if prepaid, if not prepaid S&H depends on quantity ordered

Presents a methodology for quantifying the health risks associated with exposure to environmental and occupational toxins. Covers the characterization of exposure of a risk group; evaluation of experimental studies; calculation of risk and cases; and calculation of acceptable concentrations of toxins. Also contains examples of risk assessments. Requires only a basic knowledge of biology and algebra to use the methodology presented.

Registry of Toxic Effects of Chemical Substances, 1985-86 Edition. National Institute for Occupational Safety and Health. Washington, DC: G.P.O., 1988.

U.S. Government Printing Office
Superintendent of Documents
Washington, DC 20402

202-783-3238
FTS 783-3238

U.S. G.P.O. #017-033-00431-5 $85.00

Lists prime chemical name substances with their associated toxicity data; includes all substances for which regulatory or consensus group information is cited. This edition replaces and updates the older printed versions of RTECS.

Research to Improve Health Risk Assessments (RIHRA) Program. U.S. EPA, Office of Research and Development, Washington, D.C. 20460.
EPA/600/8-88/089

Center for Environmental Research Information
U.S. EPA
26 West Martin Luther King Drive
Cincinnati, OH 45268

513-569-7562

Presents plan for integrated and systematic research program to reduce uncertainties, due to deficiencies in the quality and quantity of appropriate data, in health risk assessments. Describes targeted laboratory and field research to improve health risk assessments.

Risk Assessment in the Federal Government: Managing the Process. Committee on the Institutional Means for Assessment of Risks to Public Health, Commission on Life Sciences, and National Research Council. Washington, DC: National Academy Press, 1983.

National Academy Press
2101 Constitution Avenue
Washington, DC 20418
202-334-3313

National Academy: $14.50; 15% discount over 4 copies; S&H (book rate) included in price

A Congressionally-mandated study by the National Academy of Sciences to determine institutional mechanisms for strengthening risk assessment as the basis for federal regulatory policies. Explores the relationship between science and policy in risk assessment. Discusses the current practice of risk assessment and its relationship to the process of regulation; past efforts to develop risk assessment guidelines; experiences of regulatory agencies with different administrative arrangements for risk assessment; and various proposals to modify risk assessment procedures.

The Risk Assessment Guidelines of 1986. U.S. EPA, Office of Health and Environmental Assessment, Washington, DC 20460.
EPA-600/8-87-045
NTIS PB88-123997/AS.

Center for Environmental Research Information
U.S. EPA
26 West Martin Luther King Drive
Cincinnati, OH 45268
513-569-7562

Presents the U.S. EPA's risk assessment guidelines relating to five areas: carcinogenicity, mutagenicity, chemical mixtures, suspect developmental toxicants, and estimating exposure. Presents the five guidelines as they originally appeared in the *Federal Register* (51 FR 33992-34054) but in a format that is easier to read.

Stedmans Medical Dictionary, 24th ed. Williams and Wilkins Co., Baltimore.
ISBN:0-683-07915-8

Williams and Wilkins Co.
428 E. Preston Street
Baltimore, MD 21202
301-528-4000

Williams and Wilkins: $36.95 ea; no quantity discounts, S&H $7.34/copy.

A widely used, comprehensive medical dictionary.

Superfund Public Health Evaluation Manual, U.S. Environmental Protection Agency. U.S. EPA Office of Emergency and Remedial Response, Washington, DC, 1986b.
EPA-540/1-86/060.

Order from EPA Public Information Center 202-382-2080

(Note: This document is currently being revised; new edition will be available Fall 1989.)

Establishes a framework for public health evaluation at Superfund sites and for development of health-based performance goals for remedial alternatives based on applicable laws or risk analysis techniques.

Threshold Limit Values and Biological Exposure Indices, 1986-1987 ed.
American Conference of Governmental Industrial Hygienists (ACGIH).

American Conference of Governmental Industrial Hygienists
6500 Glenway, Bldg. D-7
Cincinnati, OH 45211
513-661-7881

ACGIH: $4.50/1-4 copies; $3.50/5-9 copies, $3.00/10-49 copies, $2.75/50-199 copies; S&H depends on quantity ordered

A pocket-sized listing of chemical specific exposure limits for the workplace recommended by the ACGIH. Contains over 400 chemical listings for Threshold Limit Values (TLVs) and approximately 16 chemical listings for Biological Exposure Limits (BELs).

Also see:

Documentation of Threshold Limit Values and Biological Exposure Limits, 5th ed., 1986. ACGIH.

American Conference of Governmental Industrial Hygienists
6500 Glenway, Bldg. D-7
Cincinnati, OH 45211
513-661-7881

ACGIH: $110/1 copy, $99/5-15 copies; $88/16 or more copies; no S&H charges if prepaid

Provides detailed documentation for chemical-specific exposure limits recommended by the ACGIH. Gives the chemical formula, statement on toxicity and hazards, explanation of the basis for selection of the TLV, and references for each substance.

Toxicology: A Primer on Toxicology Principles and Applications, Michael Kamrin. Chelsea, Michigan: Lewis Publishers, Inc., 1988.
ISBN:0-87371-133-5

Lewis Publishers, Inc.
121 S. Main Street
P.O. Drawer 512
Chelsea, MI 48114
800-525-7894

Lewis: $27.50; no quantity discount; S&H $3.00 to $5.00

Discussion of the general principles of toxicology; toxicology in risk assessment and risk management; and analysis of four case studies.

User's Manual for the Human Exposure Model (HEM), U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC, 1986.

Federal, State, and local agencies can obtain free copies by contacting the Pollutant Assessment Branch, Office of Air Quality Planning and Standards at 919-541-5647; FTS 629-5647.

Describes the Human Exposure Model (HEM), a general model designed to estimate the population exposed to air pollutants emitted from stationary sources and the carcinogenic risk associated with this exposure. Explains the use of the two basic models within HEM, the System Applications Human Exposure and Dosage (SHED) model and the Systems Application Human Exposure and Risk (SHEAR) model.

☆U.S. GOVERNMENT PRINTING OFFICE: 1989-648-163/87084

United States
Environmental Protection
Agency

Center for Environmental Research
Information
Cincinnati OH 45268

BULK RATE
POSTAGE & FEES PAID
EPA
PERMIT No. G-35

Official Business
Penalty for Private Use, $300

Please make all necessary changes on the above label, detach or copy, and return to the address in the upper left-hand corner.

If you do not wish to receive these reports CHECK HERE ☐; detach, or copy this cover, and return to the address in the upper left-hand corner.

EPA/450/3-88/016